The New England
Journal of Medicine

Copyright, 1939, by the Massachusetts Medical Society

VOLUME 221 NOVEMBER 16, 1939 NUMBER 20

MASSACHUSETTS MEDICAL SOCIETY

Section of Dermatology*

THE WAR AGAINST SYPHILIS

E. LAWRENCE OLIVER, M.D.†

BOSTON

THE history of syphilis is the most dramatic story in the history of disease, and its control is one of the most important sanitary problems in medicine. The portion of this paper concerning the history of syphilis is based largely on that admirable book, *The History and Epidemiology of Syphilis* by William A. Pusey,[1] which was published in 1933.

Syphilis appeared in Europe with explosive suddenness at the end of the fifteenth century. In 1494, Charles VIII of France sent his troops into Italy with the object of capturing Naples, which object was attained February 22, 1495. During the next few months, a new disease broke out with such violence among his troops that before the spring of 1495 was over his army was forced to abandon the city and retreat in confusion. These troops, scattering over Europe, sowed the seeds of the disease wherever they went, so that within the short space of two years the malady had spread with astounding rapidity over most of Europe, including the British Isles. The fight against syphilis began at that time. Bloch states that in 1496 the Parliament of Paris decreed that all persons infected with the disease should leave the city within twenty-four hours. The next year the Privy Council of Scotland passed a law ordering banishment to the island of Inchkeith for all the inhabitants of Edinburgh who were victims of the disease.

At this time the new disease had no exact name: the Italians called it the French disease; the French called it the Italian disease; the Russians called it the Polish disease. However, all believed it was a new disease which had not previously been encountered in Europe. Whence did it come? There is much to indicate that the disease came from the New World, having been brought to Europe by the sailors of Columbus. No description of the syphilitic syndrome has been found prior to 1493. The first Spaniards who recognized syphilis called it the disease of Española, which signified the disease of Haiti. Another very potent reason for believing that syphilis was a disease new to Europe was its malignity during the first fifty years after its explosive outbreak. The high fever, the intense pains in the joints, the severity of the rash, the even frequent death in the secondary stage, all point to a disease to which Europeans had acquired no natural immunity.

For written evidence that syphilis came from the New World we have the work, printed about 1515, of Diaz de Isla, who was a practicing physician in Barcelona in 1493. He states that syphilis was unknown in Europe before 1493, that its home was in Haiti, and that he himself had treated several of Columbus's sailors soon after their arrival in Barcelona in 1493.

From Europe the disease spread to Africa and the Orient. The researches of Okamura and Susuki for Japan and China and those of Jolly for India indicate that syphilis appeared in those countries only after contact with Europe. In India the disease was recognized in 1498 after the arrival of Vasco de Gama, who had left Portugal in 1497.

Mercury was employed as a remedy very early in the history of syphilis. This is not surprising, as mercury had been used for a long time by Arabian physicians in leprosy and psoriasis. Paracelsus is given credit for its first use in the treatment of syphilis.

*This section meeting was held and the following three papers read during the annual meeting of the Massachusetts Medical Society, Worcester, Massachusetts, June 6, 1939.

†Clinical professor of dermatology and syphilology, emeritus, Harvard Medical School; member of Board of Consultation, Massachusetts General Hospital, Boston.

In the seventeenth and early eighteenth centuries most if not all the lesions of syphilis had been gumma, syphilitic meningitis and lesions of the bones, spleen and kidneys. Lancisi before 1720 had noted a relation between diseases of the heart and blood vessels, including aneurysm, to syphilis. Before the end of the eighteenth century hereditary syphilis was well known. Extragenital chancres were recognized, and the dangers of contagion by kissing or from contaminated drinking cups were emphasized.

Wallace, of Dublin, in 1834 was the first to introduce potassium iodide in the treatment of syphilis.

In 1905 Schaudinn and Hoffmann discovered the *Treponema pallidum*, and in 1906 Wassermann and others demonstrated the value of serum tests in the diagnosis of syphilis. Three years later Ehrlich began the use of arsphenamine in treatment. At first it was believed that one treatment with arsphenamine would cure the disease. Though this theory soon was shown to be fallacious, nevertheless arsphenamine has remained the most valuable drug in the treatment of the disease.

The value of personal prophylaxis by the use of 33 per cent calomel ointment within a few hours after exposure was demonstrated by Metchnikoff[2] in 1906. The results of this method of prophylaxis in the United States Army during the World War were amazing. It is unfortunate that this method is not better known. As Pusey says:

> Any method of this sort has been regarded by a part of the community as immoral and an encouragement to sexual license. If syphilis is to be regarded as a proper punishment for sexual irregularity, then all attempts to prevent its spread are unjustifiable and the whole effort against it falls to the ground. But it is hard to believe that intelligent men and women that pretend to be humane will, as a class, accept this attitude.

It is probable that no other measure for the control of syphilis would be as valuable as the wide diffusion of knowledge as to the extraordinary value of 33 per cent calomel ointment, if used within five hours after exposure.

In regard to laws designed to control syphilis, the Swedish Act[3] of 1918 has proved so successful that it has drawn the attention of the entire world. During the sixteen years following the passage of this act, the number of cases of early syphilis in Sweden fell from the rate of 10 in every 10,000 population to less than 1.

The principal features of this act have been summarized as follows: Every person suffering from venereal disease must submit to medical treatment and follow instructions. Such treatment can be furnished only by a qualified practitioner. Free treatment is provided for those who need it. All cases not previously treated by another physician must be forthwith reported to the local inspector of health, but without divulging the patient's name. The name is to be entered on the physician's record but is not reported to the authorities unless the patient defaults in treatment or unless for some other reason coercive measures are called for. The obligation rests on the physician to ascertain the source of infection if possible and to convey the name and address of such alleged source, when obtainable, to the local inspector of health, who then takes steps to have the person examined.

In Norway there is no free treatment of syphilis except for sailors and indigents.[3] The government has considered adopting the Swedish law, but the expense of carrying out the provisions of such a law has so far prevented its adoption.

In Holland there is no notification of cases and no compulsion to undergo treatment, but since 1925 much valuable work has been done by social workers, health visitors and nurses, who endeavor to see that patients are properly treated and followed up.[3]

In England efforts to control syphilis go back to 1875, but it is only since 1914 that free treatment has been available to every syphilitic patient regardless of financial status.[3] In 1935 there were 185 treatment centers in England and Wales and 52 in Scotland. Patients may be urged to continue treatment, but there is no compulsion. They may discontinue treatment at any time, the British principle being that personal liberty and freedom of action must be respected. Education of the public in regard to venereal diseases by wide advertising of the venereal clinics is an important factor in the British plan.

Although figures indicate a considerable decrease of early syphilis in England—a 34 per cent drop from 1931 to 1935—it is believed by some that these figures are misleading, as an ever-increasing number of syphilitic patients treated by private physicians do not appear in the official records.

The extraordinarily successful results of the law in Sweden are probably due to the fact that the Swedish public has a marked respect for the law and the medical profession. It is certain that respect for the law is not one of the American virtues. We all know how little respect was paid to the Prohibition Amendment.

For some years many of our states, Massachusetts among them, have had laws more or less similar to those of Sweden, providing that all cases of syphilis shall be reported to the health authori-

ties, but without names or addresses. If patients stop treatment against advice they become reportable by name and address.

Successful results from such laws naturally depend on its administration and on the co-operation of physicians. Since the passage of this law in Massachusetts, statistics indicate a marked decrease in the incidence of early syphilis, with an increase in the number of late cases that would naturally be expected with the wider use of serum tests.

Since Surgeon General Thomas Parran in 1936 started his campaign to bring the problem of syphilis control to public attention, the American public is demanding laws designed to safeguard marriage and the unborn child.

In the *Journal of Syphilis, Gonorrhoea and Venereal Diseases* for May, 1939, there is a summary of a debate on the value of such premarital examination laws, Dr. William Snow, upholding them, and Dr. N. A. Nelson, director of the Division of Genitoinfectious Diseases, Massachusetts Department of Public Health, opposing them. Snow's arguments are as follows:

The laws constitute a valuable method of case finding, the first essential in any program for the control of syphilis.

They will decrease the transmission of syphilis in marriage.

They will decrease the incidence of congenital syphilis.

By insistence on blood tests by "approved laboratories" they will raise the standard of laboratory performance throughout the country.

They will have a general educational value in keeping the problem of syphilis closely in the public mind.

Nelson's arguments are these:

In the diagnosis of syphilis emphasis is laid almost wholly on the laboratory.

The specificity of serological tests for syphilis in the best of hands is technically short of perfect. False positives in supposedly good laboratories have been estimated at times at as high as 10 per cent.

In two reasonably prevalent diseases in this country (malaria and infectious mononucleosis), biological false-positive results occur in a significant proportion of cases, and far too little positive modern information is available as to biological false-positive tests in many other conditions. Moreover, evidence is accumulating which suggests that the blood of a small but as yet unknown proportion of perfectly normal persons may from time to time, or permanently, contain enough reagin or reagin-like substance to cause a transitory or permanent biological false-positive serological test. Therefore, a considerable number of non-syphilitic persons will be caused undue harm, delay in marriage and expense due to the unraveling of the significance of false-positive or doubtful results. The case reports of Stokes and Ingraham[4] make clear that this is already happening.

The blood test is a wholly invalid indicator of infectiousness or non-infectiousness in syphilis.

The law will not serve its purpose in preventing the spread of syphilis within marriage. Premarital intercourse is already so frequent as to make the law an effort to lock the stable door after the horse has been stolen. In the social and economic groups having the highest incidence of syphilis, the incidence of common-law marriages and illegitimacy will be increased.

Regardless of arguments for or against premarital examination for syphilis, it is evident that laws of this kind will soon be passed in most of our states. It would seem, then, to be the part of wisdom for our medical societies to take a larger part in this type of legislation, and to approve such laws as leave the decision as to infectiousness in the hands of the physician, where it belongs; for it is the physician who will see and examine those desiring marriage. It is the physician who is best able to evaluate the result of the blood test and best qualified to give advice on the question of marriage if the test is reported positive. The Committee on State and National Legislation of the Massachusetts Medical Society has recently gone on record as approving such a law for our state.[5]

There are now premarital examination laws in twenty-six states of the Union. In three states (Illinois, Michigan and Kentucky) marriage is forbidden to all persons showing positive serological tests.[6] It would seem that the passing of such laws must be due to a combination of ignorance and mass hysteria. It is conceded by syphilologists the world over that a positive test is no criterion of infectiousness. If human rights are to be totally disregarded and if this hysteria keeps growing at the present rate, it would be hardly surprising if a law were suggested demanding universal blood tests, with euthanasia for all those with positive reactions. Such a law would prove effective but, to say the least, would be a bit unfair.

Five states now have laws requiring the reporting of the names of all patients with syphilis. It is probable that such laws will prove worse than useless. Patients with venereal diseases desire secrecy above all; reporting them by numbers does not disturb them, but they do not like the idea of having their names placed on the files of public authorities. Such laws encourage timid patients to attempt self-treatment or to go without any treatment, thus prolonging the period of their infectiousness. Of course their names are supposed to be kept in inviolate secrecy, but state secrets have been known to leak out in the past. Even blackmail would seem to be a possibility if the names should come to the attention of an unscrupulous individual employed by a department of health. Statistics of the disease in states with such laws are apt to be worthless, for many physicians, believing in the sanctity of privileged communications, will not obey such laws.

As regards the relation of syphilis to pregnancy, New York in 1938 was the first state to pass a law requiring that blood tests be made on all pregnant women. Several years ago an investigation[7] had shown that although the public clinics in New York were doing blood tests on all pregnant women, only about half the physicians attending private obstetric cases were testing their patients.

Treatment of pregnant women with syphilis is notably successful in preventing congenital syphilis, provided the patient is seen before the fifth month of pregnancy. In many maternity hospitals the incidence of congenital syphilis has been greatly reduced since blood testing has been the rule. If a considerable number of cases of congenital syphilis can be prevented by such laws, there is little reason to object to them for any cause other than the expense of administration.

In the war against syphilis, the public should be made to realize the wide prevalence of the disease. It should be taught that there are efficient means of prevention; that there are efficient methods of diagnosis and treatment; that the earlier a case comes under treatment the greater the probability of a cure, without minimizing the fact that treatment is of great value in all stages of the disease. It should also be shown that hereditary syphilis may be practically abolished if women with the disease are placed under efficient treatment before the fourth or fifth month of their pregnancy.

If it be conceded that the control of syphilis is one of the most important problems in medicine, it is evident that considerably more time should be allotted for instruction concerning syphilis in our medical schools.

If the public can be taught the value of prophylaxis, as well as the importance of early diagnosis and treatment, if the medical profession as a whole is made to realize the importance of sufficient treatment, especially in the early stages of the disease, and if the fight is not hampered by ill-advised and unenforceable legislation, it is hoped and believed that rapid progress will soon be evident in the war against syphilis.

20 Fairfield Street.

REFERENCES

1. Pusey, W. A.: *The History and Epidemiology of Syphilis: The Gehrmann lectures, University of Illinois, 1933.* 113 pp. Springfield, Illinois and Baltimore: Charles C Thomas, 1933.
2. Metchnikoff, E.: Sur la prophylaxie de la syphilis. Ann. Inst. Pasteur **21**:753-759, 1907.
3. Report of the New York City commission to investigate the prevention and control of syphilis and gonorrhea in Scandinavian countries and in Great Britain. Am. J. Syph., Gonor. & Ven. Dis. **20**:7-63 (Supp. July), 1936.
4. Stokes, J. H., and Ingraham, N. R., Jr.: Syphilis and the law, with discussion of false positive blood serologic test. J. A. M. A. **112**:1133-1143, 1939.
5. Lund, C. C.: Control of syphilis. New Eng. J. Med. **220**:648, 1939.
6. Nelson, N. A.: personal communication.
7. Exner, M. J.: Syphilis in pregnancy: report of a study. J. A. M. A. **106**:488-490, 1936.

LUES LATENS*

PAUL A. O'LEARY, M.D.†

ROCHESTER, MINNESOTA

A FEW moments' reflection will bring to light the fact that the bulk of our knowledge of syphilis has been acquired during the last twenty-five years. Although the debate continues as to whether Columbus imported the disease to Europe on the return from his second trip to this country or whether it had existed on the Continent before his time, the information gathered during the last few years has materially changed our conception of a disease that has been prevalent for more than four hundred years. During the quarter of a century that has gone we learned of the limitations of the drugs which were originally thought to be, or at least were hoped to be, panaceas for a disease which requires from fifteen to twenty years to develop its serious sequelae. If the physician who became interested in syphilis when the arsphenamines were first introduced has recently had either the opportunity or the incentive to survey the patients who were well treated twenty years ago, he will find that, although some of them may still react positively to a blood test, very few manifest any of the late complications of the disease. A terse statement of the accomplishment of the modern treatment of syphilis, as a result of surveys by the Co-operative Clinic Group,[1–6] may be briefly summarized as follows: although intensive specific treatment of early syphilis does not cure all patients, it does prevent the development of the late complications of the disease in all but 2 per cent of the patients treated. It is obvious, then, that although our efforts are still directed toward cure, and whereas this is accom-

*From the Section on Dermatology and Syphilology, Mayo Clinic, Rochester, Minnesota.

†Head of Section on Dermatology and Syphilology, Mayo Clinic, Rochester, Minnesota; professor of dermatology and syphilology, Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota.

plished in approximately 85 per cent of the cases, the fact that it is possible to prevent the appearance of the incapacitating and death-dealing complications in 98 per cent of the patients is the basis for the present state of enthusiasm for the intensive treatment of early syphilis. For many years the thought of cure was limited to cases in which treatment was started during the early phases of the disease, but we now recognize that cure is also possible when the patient begins treatment after the disease has been present for some years. Likewise, it is now established that spontaneous cure occurs in approximately a third of the cases in which the disease is acquired.[7] Such cures occur in cases in which patients do not receive any treatment whatsoever for syphilis. Since the period of observation following malarial therapy in many cases is now more than fifteen years, there is substantial evidence at hand that cures also occur after this type of treatment in cases with types of neurosyphilis which were unresponsive to any therapeutic program previous to the fever-therapy era. The basis for this statement is the result of the pathological studies of the brains of patients with general paresis who were treated with malarial therapy ten or more years ago.

The means of estimating cure in a case of syphilis are based on clinical observation for at least five years after the patient has become clinically and serologically negative.[8] Serologic negativity applies to both blood and spinal-fluid tests. With each year after the expiration of the five-year period that the patient continues to remain clinically and serologically negative, the likelihood of cure becomes greater.

Before discussing latent syphilis or latency, a brief résumé of the present-day conception of the course of the disease would seem advisable. For the expressions "first," "second" and "third" stages have been substituted "early" or "acute," "latent" and "late" syphilis. The reason for adopting these terms is the more thorough understanding of the biological course of the disease. The period of early or acute syphilis includes the first two years, the period in which the patient is infectious and during which the majority of the relapses of all types occur. Unfortunately it cannot be said that all patients cease to be infectious at the end of the second year, because one occasionally encounters individuals who maintain infectious lesions for many years. However, such cases are not common and are becoming rare.

Latent syphilis follows early syphilis, and is characterized by the absence of clinical signs and symptoms of the disease. The real significance of the period of latency depends on whether it remains as a permanent state or is only temporary.[9] In those cases in which latency is temporary, late syphilis may appear in the form of cardiovascular disease, neurosyphilis, osseous or cutaneous lesions or any of the other numerous late manifestations.

Latency may be defined as that period of the disease, after the disappearance of the signs of acute syphilis, when the patient is free of both signs and symptoms. Latency has been subdivided into early and late types. Early latency includes the third and fourth years, while late latency embodies the period beyond the fourth year in which the patient remains free of clinical evidence of the disease. The significance of early and late latency will be elaborated on subsequently.

Latency has been further classified by Moore and others[2] into clinical, serologic and pathologic types. Clinical latency is that phase characterized by a complete absence of clinical signs or symptoms of syphilis. Serologic latency implies that although the results of serological tests are negative there are still foci of active syphilitic disease in the patient. Pathologic latency denotes an asymptomatic phase of the disease in which, however, nests of *Treponema pallidum* have become walled off in one or more of the viscera, but no pathologic reaction has developed in situ as a result.

Of the types encountered by physicians, clinical latency is the most frequent, and its importance overshadows the other types from the clinician's and patient's viewpoints because it offers a variety of problems in its management. In reality, however, the pathologic type of latency is more important, because the subsequent course of the disease is dependent on the activity of the biologic processes. Many of the patients who acquire syphilis have a chancre, followed by lesions on the skin and mucous membranes. By no means do all these patients have an obvious chancre and the subsequent cutaneous manifestations of the disease, and many of them pass through the early phase of syphilis without displaying clinically recognizable manifestations of these commonly anticipated signs. Perhaps the chancre may be so small as to pass unnoticed or the cutaneous symptoms so mild that they are not recognizable. Following the involution of the early signs of the disease, either as the result of treatment or spontaneously, the patient then passes into the period of early latency. His defense mechanism, if it is active, has by this time started to function, with the result that he does not display further evidence of the disease. Within a period of another two years he passes into the phase of late latency. If during the early stage of the infection the individual's defense mechanism is lacking, either from inherent

qualities, inadequate treatment or virulency of the organism, he does not slip through the early period so asymptomatically. He may have lesions on the skin or the mucous membranes which continue to be a source of infection to others, or he may manifest evidence of recurrence of the disease in the central nervous system, viscera or one of the organs of special sense. These recurrences may show a rapid response to treatment, or they may be the forerunners of a serious course of events which result in the patient's incapacity or death.

Comment has been made that latency which is only of a temporary nature is a serious form of syphilis, for the following reasons. The acute signs subside either spontaneously or as a result of treatment, and the patient passes into the early phase of latency. He is asymptomatic, and hence feels well and either forgets or minimizes the fact that he has syphilis; however, during the period of the acute syphilis, invasion of the central nervous system or the viscera by the *Treponema pallidum* has occurred. A pathologic reaction takes place at these sites, and some ten or more years later the patient presents clinical signs that the organ has become definitely involved by the syphilitic process. In other words, although the patient has been without symptoms of the disease during this ten-year period, the infection has been present in an asymptomatic form and all the while amenable to treatment. This serves to emphasize one point in particular, namely, that the invasion of the various systems takes place at the time of the dissemination of the spirochetes during acute syphilis, although the clinical evidence of involvement may not become obvious for several decades. Thus it is understandable that the term "temporary latency" is synonymous with asymptomatic syphilis. In contrast with the course of events just described is the case which passes through the early phases of the disease to a state of latency that remains permanent. Such patients never manifest signs of syphilis of the central nervous system, viscera or other organs but continue to remain asymptomatic during the remainder of their lives. The patients who are fortunate enough to maintain this state may do so as the result of treatment or spontaneously, perhaps as the result of an efficient defense mechanism against the disease. The fact that a permanent state of latency develops in some cases does not mean that invasion of one or the other of the various systems did not occur. It does mean, however, that even though such invasion took place the spirochetes were walled off or destroyed in situ so that a pathologic reaction at that point did not develop. The observation of a large group of patients with early syphilis and invasion of the central nervous system as evidenced by a positive reaction of the spinal fluid has revealed that many of them will overcome this invasion, that the reaction of the spinal fluid will become negative and that signs of neurosyphilis will subsequently not be demonstrable.

Hence, it may be said that a patient who is not cured of the disease during the acute phase does well to obtain a permanent state of latency. It may also be said that permanent latency, from the patient's viewpoint, is equivalent to cure.

Serologic latency implies that although the results of serological tests are negative the patient still has active foci of syphilis. This was a common finding in the period of the old serological technics, but now with the newer flocculation procedures the incidence of serologic latency is becoming less. With the development of more sensitive tests which the future will no doubt bring, the patient with serologic latency will become rare.

Pathologic latency means that active *Treponemata pallida* are present in tissue but that a pathologic reaction on the part of the host to the invader, in the form of minute or massive gummas, is lacking. Warthin fostered this conception of latency, and by so doing has prevented enthusiastic syphilologists from speaking too glibly of the incidence of cure in a group of patients treated and observed clinically. Warthin's conception of pathologic latency is still a subject for debate and its proof is dependent on the findings at necropsy.

The diagnosis of latency is based on the following: the history and the approximate date on which the infection was acquired; a negative reaction of the spinal fluid; absence of clinical signs or symptoms of syphilis, especially in the central nervous or cardiovascular system; some knowledge of the type and amount of treatment previously given; a negative or positive result of a flocculation test on the blood; and the opportunity for frequent clinical re-examinations.

It is of value to know the duration of the disease in appraising the state of latency; hence, some information as to the date on which the acute signs of the disease were recognized is essential. Unfortunately, these data are obtainable in only about half the cases; therefore the historical information starts from the time that a positive result with a serological test was obtained. The advantage of having definite knowledge in regard to the duration of the disease permits one to classify the patient in either the early or late phase of latency. Early latency is of less significance than late latency because the former is of short duration, while the latter becomes greater each year that the patient retains latency as a permanent state. An individual who has had syphilis for twenty-five years and is found to be asymptomatic

will in all probability remain so. The same, of course, cannot be said of the patient in whom the disease has been present only four years.

A negative reaction of the spinal fluid is essential for a diagnosis of latency. If this is found in a case in which syphilis has been present for more than five years, the patient can be assured to the extent of 99 per cent that the spinal fluid will always remain negative; however, if the disease has been present for less than five years this assertion cannot be made until sufficient time has elapsed and a subsequent examination of the spinal fluid at the end of the course of treatment has been made and has given a negative result. In a case in which the reaction of the spinal fluid was positive at the time of the acute syphilis, repeated examinations of the fluid are necessary for a period of five years, especially if the results of tests on the blood remain positive or if a change from negative to positive occurs.

The diagnosis of latency cannot be made if the patient displays any signs or symptoms of syphilis. Likewise, in some cases, especially those in which historical data are lacking, such a diagnosis cannot be made at the time of the first clinical examination, even though such examination does not disclose any manifestations of syphilis. As the disease is prone to involve almost any of the organs of the body, a complete clinical survey is essential, although special scrutiny should be directed to the cardiovascular system. A roentgenographic examination of the heart and aorta is essential, and even though the report is negative the roentgenogram should be kept as a part of the patient's record for future comparison. In addition, careful examination of the pupils, the deep tendon reflexes, the mucous membranes, the liver, the hearing and the osseous system should be made not only at the original examination but also at each subsequent examination of the patient. It is only by such re-examination that it is possible to demonstrate that the patient has the permanent state of latency.

Some knowledge as to the type and amount of treatment previously received is also of aid in recognizing the state of latency. Although this information is of special value in determining the subsequent course of treatment to be followed, it is also a guide to the status of the patient's defense mechanism. The individual who has received more than the average amount of treatment usually given in cases of acute syphilis — thirty injections of arsphenamine and sixty injections of bismuth — and still manifests evidence of syphilis is lacking in his forces of resistance, whereas the individual who has received only four or five injections of arsphenamine and a few injections of bismuth and shows no signs of infection probably has an active defense mechanism. For these reasons some information about previous treatment is of value.

Little has been said thus far about blood tests. The reason for this is that the diagnosis or the treatment of latency is not dependent on the status of the reports of flocculation tests on the blood. In many cases in which the disease is in the permanent state of latency the results of blood tests are persistently positive but the patients never have any manifestations of late syphilis. In a small percentage of cases of active visceral syphilis the results of tests on the blood are negative. Accordingly, the results of flocculation or complement-fixation tests on the blood are not a significant guide in determining the status of a patient with the latent type of syphilis. The significance of a change in the results of blood tests from positive to negative in a case of latent syphilis in which the patient has been under observation for several years grows in proportion to the number of years the results of the tests remain negative. When the opposite occurs, that is, when the result of a test has been negative for some years but becomes positive, a painstaking clinical re-examination should be made in an effort to find the place in which syphilis has become active. If the syphilis has been present for five years or less, the spinal fluid should be re-examined.

Frequent re-examinations of the patient with latency are essential to adequate care and supervision. For the first two years after treatment is stopped these clinical surveys should be made at intervals of six months, and thereafter should be made annually until the disease has been present approximately twenty years. This period is selected because it is known that the majority of the serious complications of the disease are recognizable by the fifteenth year after the infection has been acquired.

The treatment of latency cannot be systematized as can the treatment of early syphilis. The individualization of the therapeutic program in each case is necessarily based on such factors as the sex and age of the patient, the duration of the syphilis, the amount and type of previous treatment and the patient's attitude toward the disease.

If the disease has been present for thirty or forty years, if the patient is sixty years or older, if the disease is asymptomatic and if a positive result of a flocculation test is the only evidence that the patient has syphilis, treatment is not warranted. Such a patient is not infectious and has long since passed the period at which complications are likely to develop. One should minimize or ignore the positive results of the blood test in such a case.

If the patient is a young woman who has had the disease for five or six years and has been in-

tensively treated during early phases of the disease, and if the result of a flocculation test on the blood is still positive, the administration of two courses of bismuth a year, twenty injections to the course, should be given for at least three and preferably for the next five years. If, however, the young woman has not been treated during the acute phase of the disease she should receive intensive therapy with arsphenamine and bismuth; at least the minimum course of thirty injections of arsphenamine and sixty injections of bismuth should be given by either the continuous or the intermittent method of treatment. Latent syphilis in a woman in the child-bearing period of life requires entirely different treatment than does latency in the male. If such a woman becomes pregnant she must be treated intensively throughout the pregnancy, because in approximately 20 per cent of the women with latency the pregnancy is interrupted by the disease or the child is subsequently found to have syphilis.

Between the examples cited of the patient who is sixty years of age and the young woman are the great bulk of patients who have latent syphilis and who seek negative serological tests and the assurance that they will have no future trouble from the infection. A retrospective clinical study of a large group of these patients showed that, when observed untreated for a period of ten years, 85 per cent of the patients with permanent latency became serologically negative. The same study also demonstrated that serologic reversals appeared about the fifth year when the treatment was limited to bismuth alone. This was about half the time required when arsphenamine and a heavy metal were employed. Accordingly, in a case in which a patient acquired syphilis fifteen years previously and received only a few injections of arsphenamine at that time, a series of twenty injections of bismuth given twice a year for three years may be ample. If, however, there is a suspicion that the latency is of the temporary type, the therapeutic program should consist of the intensive use of arsphenamine and bismuth for at least the so-called minimal course. The factors already mentioned, namely the sex and age of the patient and the duration of the syphilis, rather than the results of serological tests, are a guide as to the amount of treatment to be administered. In the patient insistent that treatment should be continued as long as the results of blood tests remain positive, the semiannual course of bismuth will probably reverse the results of the tests sooner than will a combined course of arsphenamine and bismuth, and with decidedly fewer complications from treatment.

REFERENCES

1. Stokes, J. H.; Usilton, L. J.; Cole, H. N.; Moore, J. E.; O'Leary, P. A.; Wile, U. J.; Parran, T., Jr., and McMullen, J.: What treatment in early syphilis accomplishes. Ven. Dis. Inform. **15**:341-363, 1934.
2. Moore, J. E.; Cole, H. N.; O'Leary, P. A.; Stokes, J. H.; Wile, U. J.; Clark, T.; Parran, T., Jr., and Usilton, L. J.: Latent syphilis. Ven. Dis. Inform. **13**:317-331, 351-364, 371-379, and 389-401, 1932, and **14**:1-12, 1933.
3. Stokes, J. H.; Cole, H. N.; Moore, J. E.; O'Leary, P. A.; Wile, U. J.; Parran, T., Jr.; Vonderlehr, R. A., and Usilton, L. J.: Standard treatment procedure in early syphilis: a résumé of modern principles. Ven. Dis. Inform. **15**:149-161, 1934.
4. O'Leary, P. A.; Cole, H. N.; Usilton, L. J.; Moore, J. E.; Stokes, J. H.; Wile, U. J.; Parran, T., Jr., and Vonderlehr, R. A.: Tabes dorsalis. Ven. Dis. Inform. **19**:367-396, 1938.
5. Cole, H. N.; Usilton, L. J.; Moore, J. E.; O'Leary, P. A.; Stokes, J. H.; Wile, U. J.; Parran, T., Jr., and Vonderlehr, R. A.: Cardiovascular syphilis. Ven. Dis. Inform. **17**:91-118, 1936.
6. O'Leary, P. A.; Cole, H. N.; Moore, J. E.; Stokes, J. H.; Wile, U. J.; Parran, T., Jr.; Vonderlehr, R. A., and Usilton, L. J.: Asymptomatic neurosyphilis. Ven. Dis. Inform. **18**:45-65, 1937.
7. Bruusgaard, E.: Ueber das Schicksal der nicht spezifisch behandelten Luetiker. Arch. f. Dermat. u. Syph. **157**:309-332, 1929.
8. O'Leary, P. A.: Criteria of the cure of syphilis. Journal-Lancet **56**:303-306, 1936.
9. *Idem:* Latent syphilis. Minnesota Med. **19**:42-46, 1936.

Discussion

Dr. Francis M. Thurmon, Boston: In our experience in the clinics in Metropolitan Boston the cases of latent syphilis comprise approximately 60 per cent of all syphilitic cases with which we have to deal; therefore such cases constitute a very significant problem.

Insofar as the minimum amount of treatment is concerned in the early cases and their follow-up, I am in accord with using the fourth year as a dividing line, because it is usually within the first four or five years of acquired syphilis that the patient is most likely to have a serious relapse or recurrence. As Dr. O'Leary has said studies of the heart and aorta are most important, in order to gain some idea as to the condition of the cardiovascular system. I re-emphasize his statement as to the status of the blood test for syphilis; that is, the sole purpose of the test is to detect syphilis. I also concur with Dr. O'Leary's statement regarding treatment and prognosis. Emphasis must be placed on the age of the patient, the duration of the disease, and whether or not inroads of syphilis have occurred. Individual consideration is necessary for each case.

I am in complete accord with Dr. O'Leary as to Wassermann fastness. A possible consideration is whether the term might not mean a positive serological reaction in the presence of clinical evidence of syphilis. To my mind, the presence of tertiary manifestations, as Dr. O'Leary has said, is of great significance, whereas the serological test is not the problem under discussion.

THE INDICATIONS AND CONTRA-INDICATIONS OF ROENTGEN-RAY THERAPY IN DERMATOLOGY

C. Guy Lane, M.D.*

BOSTON

THE reasons for the use of radiation in skin diseases require a careful review from time to time in the light of the increased knowledge of the effect of such treatment on cells and their functions, and a re-examination of the arguments against radiation is periodically needed in view of the accumulated experience of many observers. In discussing the subject it is assumed, first, that the apparatus and technic to be used have been accurately standardized; second, that everything has been done to assure a correct diagnosis in each case; and third, that an accurate estimate has been made of those factors in the individual which influence the dosage, such as age, site, coloration and previous treatment.

X-rays are almost indispensable in dermatology but should be employed with discriminating judgment and in such a way that no harm will be produced. As with any new method of treatment, x-rays have been used too much. Progress in knowledge has advanced, and radiation therapy has approached closer to its proper place in the therapeutic field. Physicians have become more conservative as greater experience has been acquired and as newer methods have developed for the treatment of various dermatoses. It is not only poor technic but a reflection on those who practice dermatology to relieve an acne or an eczema, or cure an angioma or keloid, and years later to be confronted with a consequent atrophy, telangiectasis, pigmentation, keratosis or, in a certain number of cases, carcinoma. Many experienced dermatologists reply that radiation should be used only in conditions which it is impossible to relieve or cure in any other way. The employment of x-rays as an agent of treatment in skin disease carries with it the implication that the user has a thorough knowledge of his apparatus and its proper use. It further implies that he is entirely familiar with cutaneous diseases and the dosage required for a particular disease and case and above all knows when to stop. Treatment should always be discontinued when a disease fails to yield to a reasonable amount of treatment.

Indications

For many years the indications for radiotherapy were based on the experience of various authors as published from time to time. As time went by, the knowledge of the action of x-rays and radium on cell function was enlarged, and it became possible to base the indications for treatment more and more on fundamental structural effects accomplished by radiation. There are still numerous cases in which the indications are founded on symptomatic factors; and other cases in which physiological indications exist do not respond to exposure to x-ray or radium. It is impossible to attribute all the accomplishments of such therapy to the physiologic action of rays produced by radium or the x-ray tube. I shall, however, attempt to discuss the reasons for treatment, basing them, so far as possible, on the functional changes produced by such rays.

In the first place, there are numerous diseases in which x-rays are indicated because of the fact that they inhibit cell function. Most authorities agree that there is no stimulating effect from these rays and that the effect is always adverse. Small doses simply decrease cell function, this decrease being roughly proportional to the amount of radiation given. After a certain point, however, large doses begin to produce complete inhibition and ultimate destruction. It is well known that there is much variation in the sensitiveness to radiation of various cells throughout the body. In general it may be stated that young cells, physiologically active cells and cells of the lymphoid series are most easily inhibited. Thereafter in order of radio-sensitivity come epithelial cells, endothelial cells and those of connective tissue, muscle, bone and nerve. This inhibitory effect may be discussed with reference first to glandular activity, second to other tissues and third to hair.

In the group of physiologically active cells are found the glands of the skin — the oil and sweat glands. The effect of x-rays is well shown in the former by their ability to lessen the output of oil in seborrhea and in acne vulgaris. Not every case of acne requires x-ray therapy, and not every case treated should have the same dosage or length of treatment. Many patients do perfectly well with less than 75 r per week. Dark and oily patients and those in the older age groups are the most satisfactory patients for treatment. In acne, greater experience with radiation has reduced the dosage and defined the better types for treatment. Perhaps the percentage of cures is less, but greater safety has resulted.

*Chief of Department of Dermatology and Syphilology, Massachusetts General Hospital; lecturer, Department of Dermatology, Harvard Medical School, Boston.

Hyperidrosis and bromidrosis also respond to radiation, but at times permanent relief may not be obtained. The central-nervous-system factor is one which may not be altered by x-ray, and care should be taken to limit the dosage to amounts which will not produce any permanent changes in the skin.

Not only in the treatment of glandular tissue is inhibition produced, but also in that of other tissues. With cells of the lymphocytic group, whether in the blood, as in leukemias, or in various tissues, as in infiltrations or chronic inflammatory process, x-ray has been proved to be extremely helpful. It is found in studies of cells exposed to x-ray that the chromosome in the nucleus tends to break up, and the protoplasm to liquefy, and when dosage is carried still further the cells themselves disintegrate relatively fast. This fact applies particularly to this group, so that numerous diseases, among them leukemia, mycosis fungoides, lichen planus and psoriasis, probably respond to radiation primarily because of such changes. It is not yet possible to cure Hodgkin's disease or leukemia or mycosis fungoides, but in many cases much comfort can be given to patients with these conditions. Change in the infiltration of lichen planus is a striking example of the effect of radiation on the cells present. In mycosis fungoides, in the early stages when the lesions are thin, small doses can be given, and frequently one finds that such doses produce a remarkable change so far as symptoms and manifestations are concerned. Later, when there is much infiltration distinct granulomas appear, and perhaps when much radiation has already been given, the need for more intensive treatment and filtered treatment must be resorted to in order to keep pace with the manifestations of the disease and with the acquired resistance of the cells.

Again, in the benign types of epithelial hyperplasia the inhibitory effect of radiation is evident. In the verrucous type of lichen planus, certain warty growths and so forth, large doses, perhaps 100 to 200 r, with 0.5 to 1.0 mm. of aluminum, at intervals of ten days to three weeks, are often more helpful than small doses at short intervals.

The inhibition of endothelial cells is well shown in the results of treatment of nevi and angiomas. The short wave lengths of radium are the most effective. With adequate filtration and care to avoid any reaction, angiomas shrink and leave no trace. It is possible that the filtered rays of high x-ray voltage may produce the same result, but the difficulties of application to restless children offer a serious disadvantage.

Another inhibitory effect of x-ray concerns hair. The growth of the hair at the base of the follicle is inhibited, and after fifteen or seventeen days the hair begins to fall out, with subsequent regrowth in three or four months, provided that the physiologic amount was not exceeded. Many thousands of cases of ringworm and favus have been epilated without untoward results. Sycosis vulgaris also can be helped. Permanent epilation in hypertrichosis or hairy nevi should never be attempted. The experience of those treated according to the Tricho system is, of course, an argument against the use of x-rays for permanent epilation, but the dosage they received was probably excessive. The use of repeated epilation doses to the point of permanent epilation is a risky procedure, and eventually results in atrophy and its sequelae.

Inhibition has been discussed as the first of the physiologic effects of radiation; destruction may be considered as the second. The inhibitory action of radiation can be carried to the point of destruction. Here again the radio-sensitiveness of the various tissues is of importance. The doses of x-ray which will destroy cells of the lymphoid series, or cells with glandular activity or epithelial malignancy, are as a rule smaller than those required to destroy connective tissue or muscle. Therefore the destructive effect is most useful in the malignant type of tumors of the skin — carcinoma or sarcoma — and also in the granulomas of mycosis fungoides.

Cancerous cells must be destroyed! Biopsy and classification of the tumor in accordance with the standards worked out by Broders, the general condition of the patient and the site and tissue affected will indicate the method of attack and dosage. Six hundred to 900 r was formerly considered sufficient. The dose has gradually increased to 2000 and 2500 r or more, with various voltages and types of filtration, perhaps in one dose or in a series at short intervals. Such doses would have been considered radical a few years ago. Cases may be treated with a 100-kilovolt machine, using 1200 r unfiltered and 1200 r filtered with 1.0 mm. of aluminum, a total of 2400 r, or with a 200-kilovolt machine, using 2000 r at one sitting, filtered with 0.25 mm. of copper and 1.0 mm. of aluminum. Excellent results are obtained with each, but it seems possible that the latter may produce somewhat better results in certain thick lesions and those with involvement of cartilage.

A third physiologic action of radiation is its antipruritic effect. Many itching dermatoses respond satisfactorily, but some do not. Many cases of thickened eczema, localized pruritus vulvae, pruritus ani and so forth are relieved. Senile pruritus very frequently is also improved. The itching and thickened dermatoses, such as lichen

planus, chronic lichenified eczema and mycosis fungoides, are also relieved. It has not been my experience that the itching of dermatitis herpetiformis or urticaria has been aided by direct radiation.

A fourth possible effect of the x-ray is the relief of pain. This is not highly regarded as an indication for radiation, but in the pain following herpes zoster one finds occasionally that x-ray helps. It has also been quite striking that many patients with verruca plantaris, within two or three days of intensive therapy, during which the pain may be slightly greater, are completely relieved of any sensation of pain. This relief and that from pain in inoperable cases of cancer are undoubtedly based on another effect of the rays.

A fifth physiologic effect cannot be stated so definitely. I refer to the effect of radiation on diseases caused by bacteria and fungi. Localized pyogenic infections, as well as various types of tuberculosis, are often greatly helped. Blastomycosis, actinomycosis, tinea barbae and fungous infections of the hands and feet respond to radiation. This is apparently not a direct effect on the fungus, because the destruction of cultures requires extremely large amounts of radiation; yet very often pyogenic infections and infections from fungi respond extremely satisfactorily to proper doses of x-ray. The reason for the action in these diseases is not clear. It is possible that owing to the radio-sensitiveness of leukocytes they may be destroyed by the rays with the release of antibodies or ferments which are quickly available for defense against bacteria. It is also possible that an increase in phagocytosis is brought about by radiation. There is, altogether too frequently, a varying response in a given disease, and it is a question whether there may be more connective tissue in some cases and therefore fewer radiosensitive cells. It is also possible that chemical changes are produced in the tissue, which alter it and make it a less favorable place for the growth and action of bacteria. In the treatment of such cases filtered radiation seems to me to be more effective than unfiltered radiation.

Contraindications

Factors in the Apparatus

In discussing the contraindications of dermatologic radiation one should first of all consider factors in the apparatus. Inadequately standardized apparatus constitutes a fundamental objection to radiation. Although an epithelioma may be treated without accurate calibration, extreme care is necessary for epilation, or the treatment of acne in a blonde, or even acne in general. Any change in the machine — the replacement of a burnt-out tube, changing or overhauling the motor and so forth — requires careful checking in order to be sure that there has been no change in the amount of radiation delivered.

Another item of importance in this subject has to do with imperfectly trained technicians and assistants. The dermatologist should be absolutely sure that the technicians, assistants and graduate students to whom is entrusted the actual management of apparatus know the proper technic and are careful and accurate in carrying it out.

Idiosyncrasy

Idiosyncrasy has been mentioned as a possible item to be considered. True idiosyncrasy to x-ray is undoubtedly rare. An abnormal response to a relatively small dose has been found with other physical agents — heat, cold, ultra-violet rays. The same type of response can be produced by x-rays and radium, but these cases are unusual and their abnormal response to radiation can frequently be accounted for by other causes. Some of these causes have already been mentioned. Errors in technic, such as the omission of filtration, failure to measure accurately the target skin distance and imperfectly standardized apparatus such as I have just discussed, are possible explanations. Wrong calculation in using the arithmetical measurement of dosage possibly explains some poor results. Failure of the voltmeter seldom occurs, but there should always be two milliammeters in the circuit. Ionization-measuring apparatus is a source of possible error, both in the apparatus and in the calculation of roentgens per second. The lack of appreciation of the factors in the individual which influence dosage can often explain, in my opinion, some of the so-called cases of idiosyncrasy. Poor judgment in regard to disease and the patient to be treated decreases, of course, as a factor with increasing experience of the dermatologist in the use of radiation. Another contraindication is the lack of accurate diagnosis or the diagnosis of a condition not amenable to x-ray.

Previous Radiation

The history of previous radiation should be sought in every case in which the possibility of radiation is being considered. Under any conditions the physician should calculate and keep before him the total amount of radiation which the patient has received on a given area. The rule that not more than 4 skin units or 1200 r should be given to an area except in cancer is a safe one for the ordinary limit of radiation. But this limit has definite variations. It applies, I believe, to dark-complexioned, oily-skinned patients, but not to patients with blond skins or relatively dry skins or perhaps to treatment of the skin on

flexor surfaces. I have seen cases in which even 2 skin units or 600 r should not have been given. All erythema must be avoided if possible, and if it does occur it must be considered as a possible contraindication to further treatment. The individual patient must be considered in attempting to define an upper limit, but the total dose should never be large enough to give rise to the possibility of later changes in the skin. All previous radiation should also be considered, even after a period of some years.

In addition to those cases which give a history of having had all the radiation they ought to receive, there is another large group in which it is impossible to ascertain the exact amount already given. There are many cases in which a roentgenologist or a clinic has been asked for this information; the reply gives the dose in terms of the various factors used, without indicating the amount required to produce erythema or epilation with that particular machine, or any indication of what these factors amount to. Arithmetical computation may give a very approximate dose, but for practical purposes one is faced with a patient who has had an unknown amount of radiation, and in general it is advisable to tell him that since he did not respond to radiation previously and has nevertheless had a recurrence, it is probably best not to treat him with any further amount.

Recent radiography is another factor to be considered. The fact that dental x-ray films are being so widely used makes it necessary to inquire in our acne cases with reference to a possible additional load of radiation from this source. Many of us have seen epilation or mild erythema produced on cheeks from repeated series of dental x-ray photographs.

Conditions Producing Erythema

In general it can be said that conditions which produce a dilatation of superficial capillaries add to the risk of radiation. One hesitates to treat acute inflammatory conditions of the skin. Some infections, namely boils and carbuncles, are definitely helped by a proper amount of radiation, but the acute inflammatory conditions, especially those arising from external irritants, should not be treated by x-ray until the acute phase has subsided; and in the subacute stage relatively small doses do best, with a very gradual increase to the proper dose.

Actinic exposure is another item to be considered. Erythema produced by exposure to natural or artificial ultra-violet light calls for extreme care in radiation. It is wise to caution acne patients in the spring to avoid sunburn, and if such occurs, to omit treatment or lessen the dose.

Various chemicals increase the clinical effect of radiation in many cases, and radiation raises the threshold of erythema by these agents. Numerous lists of such agents have been published. They include iodine, tar, salicyclic acid, chrysarobin, mercury, iodoform and sulfur, and it is possible that even a greasy coating over an area treated frequently may aid in exaggerating the effect of radiation. Extremely close consideration should be given to the coincident treatment of radiated areas.

Diseases with Atrophy

Diseases in which atrophy is characteristic or in which it is an end result are in general not suitable for radiation. I am well aware that carefully selected cases of lupus vulgaris or of lupus erythematosus have been treated successfully by radiation, but in general I believe that diseases associated with atrophy are much better treated by other methods.

Diseases Not Amenable to Radiation

X-ray and radium have been used in the treatment of almost every skin disease, but there are many diseases in which they have been found to be of no value. Some of the reasons can be assumed when the known physiologic effects of radiation are considered. These have already been discussed. It is found that such widely differing conditions as erythema multiforme, urticaria, benign tumors of various types, especially those with a large amount of connective tissue, parasitic diseases and a host of others are not candidates for radiation. Eczema which has failed to respond to previous radiation should not be further treated.

Psoriasis should, I believe, be included in the group of diseases not amenable to x-ray. It does, of course, respond to x-ray, at least for a while in many cases, but the cases must be carefully selected, and the treatment limited. I have probably seen more cases of post-radiation scarring, atrophy and telangiectasia in psoriasis than in any other single disease. The recurrence of lesions, persistent requests on the part of the patient for further radiation and inadequate standardization of apparatus in years past have been large items in the production of these sad results. There are many other diseases which experience has shown are not responsive to radiation.

Patients with Blood Affections

Finally, patients with severe blood or blood-vessel affections are in general not candidates for x-ray therapy. Its effect on white blood cells and that on endothelial cells make it inadvisable in these cases. Indeed, in cases undergoing long-continued fractional treatment — those of mycosis fungoides, senile pruritus and so forth — white-cell counts

should be made from time to time in order to be sure that the number of cells remains within relatively normal limits during treatment.

Summary

If the skin diseases responding satisfactorily to radiation are carefully reviewed, it will be found that in almost all cases one or more of the following indications exist, namely the ability of the x-rays to reduce cellular activity in glands, hair or other tissues, to destroy cells, to relieve itching or pain and to act favorably on certain infections.

There are also just as definite contraindications to the use of x-ray in skin diseases. Inadequately standardized apparatus and imperfectly trained operators definitely contraindicate radiotherapy of any kind. In the individual case, previous radiation and in fact any previous recent therapy need to be carefully weighed. Conditions causing erythema call for deliberate judgment. Diseases associated with atrophy or certain blood or blood-vessel affections and skin diseases found by experience not to be amenable to radiation constitute a group not to be treated. True idiosyncrasy is relatively rare.

If radiation seems indicated in a given case the following rules should be observed: be sure that the diagnosis is correct and that the possible contraindications have been reviewed; give close attention to the details of technic; and be conservative in dosage except in cancer.

416 Marlboro Street.

Discussion

Dr. Philip Cook, Worcester: I should like to ask Dr. Lane whether he has had any experience with treating psoriasis over posterior nerve roots instead of directly over the area affected.

Dr. Arthur M. Greenwood, Boston: I am in complete agreement with Dr. Lane. I had hoped that he would also discuss a subject which was recently considered at a meeting of the American Dermatological Association — the amount of radiation absorbed by the upper parts of the skin and the type of apparatus best fitted to deliver the desired radiation. The paper on this subject, by Dr. Cipollaro, tended to show that lower voltages were better suited to skin therapy than those above 100 kilovolts.

Dr. Lane: In reply to Dr. Cook's question, I am not prepared to express an opinion on treatment over the posterior nerve roots. I have attempted it but not with entire success. In my experience, cases so treated do not respond well.

In regard to Dr. Greenwood's discussion, I too was very much interested in Dr. Cipollaro's paper, and particularly in the fact he brought out that there is so little difference between the depth doses of apparatus of voltages from 60 to 100 kilovolts. Dr. Cipollaro did some very careful work with reference to skin penetration, and found comparatively little difference in the first two or three millimeters. Within that range the absorption is apparently sufficient to give adequate therapy with various voltages.

UTERINE PROLAPSE*

The Principle of Vaginal Approach; A Preliminary Report of 465 Interposition Operations

John Fallon, M.D.†

Worcester, Massachusetts

With the warmth of deep interest, and for two thousand years, we have fought over the problem of prolapse without reaching agreement on any one of the operations so far devised. And although it has been claimed in turn for each, it is doubtful whether any one procedure constitutes the final solution. But experience with them has given us, I believe, a fundamental operative principle, a principle which has few exceptions and which gives promise of holding true for some years to come. This is that at least after the menopause we can handle prolapse by vaginal operation alone, and without laparotomy. To a gynecological society this may sound more like a platitude than a principle. However, the occasional operator notoriously, and my own colleague, the general surgeon, all too often call it heresy.

A principle so rich in practical results, which is established but not accepted, can stand repetition and the cumulation of evidence. This paper reviews some of the existing evidence and adds that of a new series of interposition operations. The report of this series is preliminary, and comparison between the interposition and other vaginal operations is purposely deferred. The comparison intended is that between abdominovaginal operations and a vaginal operation.

One might reasonably ask whether the amount of the work on prolapse and the heat of the debate are out of proportion to the gravity of the

*Read before the New England Obstetrical and Gynecological Society, May 25, 1938.

†Surgeon, Fallon Clinic and St. Vincent Hospital, Worcester, Massachusetts.

lesion. To think of prolapse as only a deformity or discomfort is to underestimate its importance. Although spectacular complications such as strangulation and progressive ulceration of the prolapsed mass are too rare to be serious hazards in the given case, more or less distortion of the sphincters, urethra, ureters and bladder — some or all — occurs as a rule. Clinically, one meets associated incontinence, frequency, burning and even acute retention. Urologic studies made on many

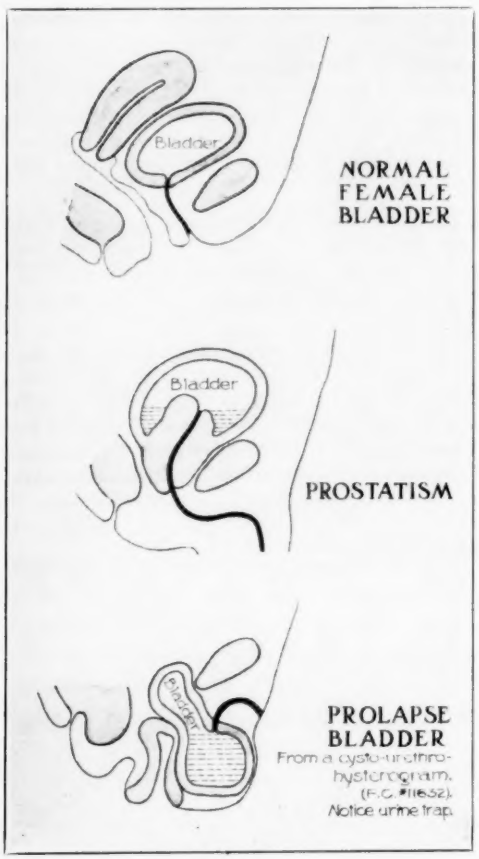

FIGURE 1.
The Prostatism of Prolapse.

of the recent patients in this clinic show a considerable incidence of obstruction and infection. The bladder mucosa is usually injected, often thickened and sometimes as trabeculated as in prostatism. There may be residual urine, hydroureter or hydronephrosis. Renal function may improve after operation, as in prostatism. Indeed it is not straining analogy to say that prolapse is the female analogue of prostatism (Fig. 1).

THE PRINCIPLE OF VAGINAL APPROACH

The common operations for prolapse fall into two major groups: the abdominovaginal, which combine vaginal plastic repair with some form of uterine suspension or fixation, and the all-vaginal. Abdominal hysterectomy is not an operation for prolapse. The visible uterus is not the disease but only an evidence of the disease in the suspensory apparatus above. Simple removal of it is quite comparable to amputation of an extremity for the pain of cord tumor and, incidentally, is followed by the most intractable recurrences.

The three principal vaginal operations are vaginal hysterectomy, parametrial fixation (Fothergill or Manchester) and interposition. In vaginal hysterectomy removal of the uterus is incidental, and the essence of the technic is the construction from the uterine pedicles of a shelf which is interposed between the bladder and abdominal viscera above and the vagina below. The Manchester suspends the cervical half of the uterus in a sling made from the uterosacral ligaments and the bases of the broad ligaments. Interposition, by drawing the fundus beneath the bladder and affixing it there, restores anteversion, changes the direction of the final component of intra-abdominal pressures and to some degree tightens the suspensory apparatus by contortion. The posterior-wall repair which is combined with each of these operations returns the axis of the vagina from the vertical toward the horizontal. If coitus need not be considered, complete vaginal closure (Dujarier and Larget) may be added to vaginal hysterectomy, or partial closure (Neugebauer-LeFort, Kahr) may be added to either vaginal hysterectomy, the Manchester or interposition.*

It is the aim of all these operations to close a breach in the complicated line of defense across the pelvic outlet, which when open permits the condition that we inadequately call uterine or genital prolapse. For a fuller discussion of the mechanics of pelvic support Farrar's[11] review and the mellow paper of Ward[22] are recommended. To summarize the subject arbitrarily, the upper ligaments of the uterus are negligible, but heredity and constitution, the hydrodynamics and aerodynamics, the leverages and the cleavage planes involved are of some importance, although they defy quick synopsis. The fixed barriers to prolapse are a lower, supporting apparatus and an upper, holding apparatus. The supporting apparatus is made up of the levatores ani and the muscular and fascial masses around the anal canal and lower vagina. These back up the front line holding apparatus and come into action when parturition, defecation or coughing threatens a break-through. Damage to these structures is not so vital as it is at the upper level.

*Kahr's[34] refinement of a possibly prehistoric operation should be better known. Essencially an exaggerated perineorrhaphy, it joins the bulbocavernosi and the sphincter vaginae muscles across the posterior five-sixths of the introitus, leaving just enough space for the urethra to empty. As simple as the Neugebauer–LeFort operation, it avoids the drag on the anterior wall which is the presumptive cause of the incontinence occasionally reported after that operation.

The upper, holding apparatus is idealized in Figure 2. It is a complex of tissues arising from the pelvic side walls and inserting all around the uterus at the level of the internal os. We confuse ourselves with names — cardinal ligaments, pubocervical fascia, pillars of the bladder, uterosacral ligaments — applied to the parts of this structure that we separate at operation. And we deceive ourselves by the memory of the tenuous films which represent these tissues in the dissecting room. It must be emphasized that they are as different in vivo as is, say, the biceps muscle.

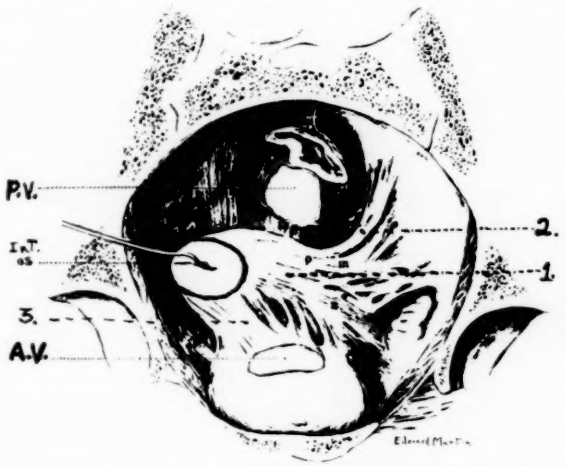

FIGURE 2. *The Endopelvic Fascia (after Martin[16]).*

The holding apparatus, the first line of defense against prolapse. The uterus has been amputated at the internal os (Int. os), *which a tenaculum pulls aside.* A. V. — *peritoneum of anterior vault;* P. V. — *peritoneum of posterior vault;* 1, 2 *and* 3 — *the cardinal, uterosacral and pubocervical ligaments, respectively.*

Although the nomenclature of this holding apparatus and some of its anatomy are still debated, its existence and its function can be easily demonstrated in the living patient. If one pulls down the cervix with a tenaculum, a finger in the vaults feels this structure tighten as the uterine excursion stops. Furthermore, in hysterectomy the uterus and upper vagina remain relatively immobile until circumcision of the cervix releases them.

The basic pathologic anatomy of prolapse has to do with failure of this holding apparatus and less directly with the loss of uterine anteversion. Vaginal hysterectomy, interposition and the Manchester operation repair this apparatus. Abdominal suspension, combined with the removal of pieces of vaginal mucosa, does not. Provided that the vaginal part of the abdominovaginal operation repairs it adequately, that is, if it approximates a Manchester, there seems to be no need of adding laparotomy, with its trauma, pain and risk.

Instead of attacking the fundamental fault, abdominal suspension furnishes a substitute mechanism. It offers a crutch, without setting the fracture. And the crutch is mechanically defective, for in recurrence after ordinary suspension the attenuated ribbon of uteroperitoneal tissue loosely connecting the site of the suspension to the prolapsed fundus bears witness that the function of uterine tissue is to stretch, and not, as suspension presumes, to withstand stretching. The demands made on suspension by simple retroversion and those made by prolapse are not comparable. In retroversion, the operation merely holds in new balance a uterus the weight of which is borne by the pelvic floor. In prolapse, suspension assumes the dead weight of the pelvic floor and the organs on it, transmitted through the uterus. Certain traumatic variations of suspension such as the suturing of a cut surface of the uterus into the rectus fascia, after excision of the fundus or splitting of the body into halves, can presumably support such a burden. But I know of no evidence that they support it better than does transvaginal repair of the damaged holding apparatus. Furthermore, suspension is a notorious cause of pelvic discomfort and internal concealed and incisional hernias. I believe, therefore, that it is not unfair to say that the abdominal part of an abdominovaginal operation helps but little and can do actual harm, especially if the anticipated help tempts the operator to slight the important vaginal part.

These more or less theoretical considerations find support in two end-result studies, chosen from the mass of such papers not for their partisanship but for their apparent detachment. The authors were, before the studies, outstanding champions of abdominovaginal operations, and had used them for the great majority of their cases.

Smith, Graves and Pemberton[21] reported 530 prolapses of procidentia degree, that is, with protrusion of the cervix through the introitus, treated by a vaginal plastic procedure combined with some kind of abdominal suspension. The mortality rate was 2.1 per cent, the number of patients followed 439, with 273 followed two years or longer. The authors classified their vaginal plastics as complete or incomplete, depending on whether all or some of the operations of trachelorrhaphy (or cervix amputation), anterior colporrhaphy and perineorrhaphy were included. The study showed: "In those cases where the incomplete plastic operation and abdominal suspension were performed, about 70 per cent were anatomic cures and about 75 per cent were symptomatic cures. When the complete plastic operation and abdominal suspension were performed about 80 per cent resulted

in anatomic cures, while about 84 per cent were symptomatically cured." Pemberton and his coworkers have since turned to all-vaginal operations.[18]

The other study, by Frank, Lindeman and Mayer, but reported by Frank,[12] apparently included some cases of lesser prolapse, presumably cystocele or rectocele alone, or uterine prolapse of less than procidentia degree. Of 480 cases treated by abdominovaginal operation 414 were followed, 231 of them eighteen months or longer after operation. The results in these 414 cases were classified as follows: good, 46 per cent; adequate, 20 per cent; inadequate, 16 per cent; poor (including 10 per cent hernia), 18 per cent. Frank called these results "extremely disappointing" and, like Pemberton, turned to the all-vaginal approach.

That these authors changed to the vaginal approach seems more significant than tabulated statistics. So many variables enter into end-result studies that few reported studies are strictly comparable. These variables are reduced, but not eliminated, in the following comparison of results after abdominovaginal and vaginal operations, by limiting discussion to one of the three principal vaginal operations.

PRELIMINARY REPORT OF INTERPOSITION OPERATIONS

Although New England gynecologists until recently have favored the abdominovaginal operation, there have been nonconformists such as Johnson and his successors at the Carney Hospital, especially Phaneuf, and my father, the late M. F. Fallon. The latter turned to the vaginal approach in 1910, and for twenty years did the interposition operation routinely for postmenopausal prolapse. His cases are of unusual value because one operator performed them all, and did them under the hardest test of any prolapse operation: that of application of the operation to every prolapse. Unlike the Smith-Graves-Pemberton series, therefore, his included a scattering few of the lesser prolapses and, unlike many interposition series, some large and gigantic ones.

The follow-up, in which Drs. Jack Meyers, Mary A. Bolger and Gerald J. Sullivan have assisted, has so far been done approximately two thirds by questionnaire and one third by examination. M. F. Fallon did 371 interposition operations, with a mortality of 2.7 per cent. Two hundred and fifteen of the patients have been followed two or more years; about 7 per cent had full recurrences, and 3 per cent had partial and for the most part asymptomatic recurrences. To the series can be added 94 more interposition operations of my own, done on selected cases of prolapses, with 1 death and no recurrences. Only 44 of my own patients have been examined after two or more years.

TABLE 1. *Interposition Results.*

YEAR	REPORTER	PLACE	NO. OF CASES	MORTALITY %	NO. OF CASES FOLLOWED	SATISFACTORY RESULTS %	COMMENT
1926	Johnson[12]	Boston	140		100	81	
1926	Cron[5]	Ann Arbor, Michigan	225	1–	183	95	13 operators
1926	Bullard[3]	New York City			77	96	
1929	Broad[2]	Syracuse	55	2	38	97	
1930	Calderon and Franco[4]	Manila	28	0			
1930	Counseller and Stacy[6]	Rochester, Minnesota	71	0	59	96	
1931	Meshberg[17]	Philadelphia	128	1–	92	92	
1933	Coventry and Moe[7]	Duluth	76		70	98	
1934	Rongy et al.[20]	New York City	501	1	398	95	8 operators
1935	Everett[10]	Baltimore	242	1.2	149	89	Include previous papers from same clinic
1935	Cattell and Swinton[8]	Boston	100+	2–	76	96	Include previous papers from same clinic
1936	Phaneuf[19]	Boston	188	2.6		±90*	
1937	Baer et al.[1]	Chicago	121	1–	83	94	
1938	Fallon (this paper)	Worcester, Massachusetts	465	2.2	259	92	
	Collected cases		8302	2.2	4453	91.4	Langanki's[15] figures, with corrections and additions

*Personal communication.

Table 1 summarizes some other series of interposition operations. Because of differences in one or more of the variables in end-result studies,—application of operation to all or only to chosen prolapses, modification of operation, number of cases, time and method of result determination, classification of results and the personal equation,—none of these are strictly comparable to the Smith-Graves-Pemberton or Frank series. The more important differences lie in the time and method of result determination and classification. However, the 259 cases in the two Fallon series which have been followed for two years or longer and checked by physical examination suggest that the com-

posite picture obtainable from Table 1 is not far from the truth.

Although the study of the Fallon cases is unfinished, certain hazards and limitations, which are no fewer than, but different from, those usually reported after interposition, have become manifest. For example, one of the commonest sources of criticism of interposition is its bladder complications, the so-called saddle bladder, interposition bladder and so on, while little is said about the mortality rate. Yet the cases in our series so far have shown a negligible incidence of lasting bladder complications, possibly because at operation the bladder was adequately freed from the uterus. Our mortality rate of 2.2 per cent seems high; however, this rate is not exceptional, for, as shown in Table 1, the 8000 collected interposition operations gave no better results. But 2 per cent certainly seems high for a vaginal operation, even though many of the patients be aged and infirm.

Listed below are the four chief faults I find with interposition, and some suggested countermoves. The first two items on the list appear to be accountable for much of our mortality.

First, actual interposition, the pulling of the fundus through the anterior wall, is usually done by tenacula, claw retractors or sutures which penetrate the uterine wall and may tear it in pulling it down. The lacerations can be serious in themselves, and they also leave portals for later infection. After devising several instruments which failed, I adopted a modified uterine sound, with the end bulbous enough to prevent puncture, which tips the fundus gently down from within.

Secondly, interposition of the large, boggy, metritic fundus, in the M. F. Fallon series, usually meant difficulty for the surgeon and discomfort for the patient, sometimes with recurrence or death. For some years, as reported to this society May 4, 1932, we have irradiated (by radium) the metritic uterus six months before operation so as to shrink and devascularize it. This has made the operation easier and therefore safer, and incidentally allowed better tailoring of the parts. Because the uterus atrophies after interposition, parts cut to fit a fundus the size of a fist will not fit the same fundus five years later, when it may be the size of a thumb.

Thirdly, interposition does not satisfactorily support the cervical stump. Since July, 1935, for more severe prolapses I have added a Manchester fixation of the cervix. Judging from the results of the 42 operations done by this method, the combination promises well.*

Fourthly and finally, it is fairly commonly recognized that interposition is not applicable to the woman who later may become pregnant. I believe we should widen this proscription and exclude the woman who is still menstruating. Pregnancy is only one of the many changes common before the menopause which, innocuous enough in a normally situated uterus, may set the scene for tragedy when the uterus is in interposition. The dysmenorrhea, the hematometra, the possibility of fibroids,[9] the inaccessibility of the endometrium to the diagnostic curet and the dangers of hysterectomy of the interposed uterus all contraindicate interposition until menstruation has ceased and the common diagnostic problems of the menopause and the possibility of fibroids are past. Incidentally, interposition with tubal ligation has probably led to more induced abortions and disastrous deliveries than have been reported. But when the surgeon is confronted by a special premenopausal prolapse which he believes he can treat best by interposition, it seems reasonable to do so and to produce the menopause by irradiation. It must be emphasized that, in this plan, irradiation is not a mere contraceptive: apart from the possibility of pregnancy, and even in the sterile woman, I believe interposition should not be done until ovarian internal secretion has ceased. The rationale of this plan is the same as that which justifies irradiational menopause for fibroids or climacteric flowing or breast cancer. I have only twice used irradiation for this indication, because prolapse hardly justifies inflicting the premature menopause, whether by vaginal hysterectomy or by irradiation-interposition, when a lesser intervention would suffice.

*This operation has since been proposed by Schumann (Surg., Gynec. & Obst. 68:481-486, 1939).

SUMMARY AND CONCLUSIONS

Uterine prolapse is too often underestimated: its urinary complications make it physiologically the analogue of prostatism. The essential lesion is a fault in the upper holding apparatus, which the principal all-vaginal operations do, and abdominal suspension does not, attack. End-result studies support this and other a priori arguments for vaginal approach. The incidences of unsatisfactory results in the series of abdominovaginal operations which are quoted were 20, 30 and 34 per cent, and in a preliminarily reported series of 259 cases followed after a vaginal operation (interposition) 10 per cent.

Since this paper is intended only to show that prolapse, or at least postmenopausal prolapse, should be handled by some vaginal operation, comparison of interposition with other vaginal operations is deferred, but certain observations on interposition are reported.

Four hundred and sixty-five interposition opera-

tions were done, with a mortality rate which was the same as that of 8000 collected interposition operations: 2.2 per cent, seemingly high for a vaginal operation.

An interposing instrument is advocated so as to avoid the trauma of tenacula to the uterine wall.

Interposition is dangerous and unsatisfactory when the uterus is large and metritic, but such a uterus can be prepared for interposition by irradiation.

Interposition does not satisfactorily support the cervical stump; however, the Manchester operation, combined with interposition, does.

Ovarian internal secretion, not merely the possibility of pregnancy, contraindicates interposition. The operation should not be done before the natural, or exceptionally an irradiational, menopause.

390 Main Street.

REFERENCES

1. Baer, J. L.; Reis, R. A., and Laemle, R. M.: Prolapse of the uterus—shifting trends in treatment. Am. J. Obst. & Gynec. **34**:827-835, 1937.
2. Broad, G. B.: Personal experience with uterine prolapse. New York State J. Med. **29**:885-888, 1929.
3. Bullard, E. A.: A study of end-results of operation for uterine prolapse at the Woman's Hospital, 1915-1925. Am. J. Obst. & Gynec. **11**:623-630, 1926.
4. Calderon, F., and Franco, C. D.: Procidentia uteri and its surgical treatment. J. Philippine Islands M. A. **10**:149-152, 1930.
5. Cattell, R. B., and Swinton, N. W.: Interposition of the uterus in the treatment of cystocele: the Watkins–Wertheim operation. S. Clin. North America **15**:1645-1652, 1935.
6. Counseller, V. S., and Stacy, L. J.: Results of various operations for prolapse of the uterus. J. A. M. A. **95**:983-988, 1930.
7. Coventry, W. A., and Moe, R. J.: Prolapse of the uterus. Am. J. Obst. & Gynec. **25**:257-261, 1933.
8. Cron, R. S.: Prevention and relief of prolapsus uteri. Surg., Gynec. & Obst. **43**:698-700, 1926.
9. Dannreuther, W. T.: Secondary sequelae after interposition of the uterus. Am. J. Obst. & Gynec. **32**:699-709, 1936.
10. Everett, H. S.: End-results with the Watkins' interposition operation. Surg., Gynec. & Obst. **61**:403-405, 1935.
11. Farrar, L. K. P.: The upper pelvic floor and its importance in total abdominal hysterectomy. Surg., Gynec. & Obst. **66**:44-54, 1938.
12. Frank, R. T.: The selection of appropriate operation for the cure of prolapse. Am. J. Obst. & Gynec. **24**:574-582, 1932.
13. Johnson, F. W.: End-results in the interposition operation for the cure of prolapsus uteri and cystocele. Surg., Gynec. & Obst. **42**:527, 1926.
14. Kahr, H.: Ein einfaches Operationsverfahren zur Zurückhaltung des Gebärmuttervorfalles bei Matronen. Zentralbl. f. Gynäk. **61**:2106-2110, 1937.
15. Langanki, H.: Ueber die Leistung der Interpositio uteri vesico-vaginalis mit vaginaler Plastik. Ztschr. f. Geburtsh. u. Gynäk. **107**:34-54, 1933.
16. Martin, E.: *Der Haftapparat der weiblichen Genitalien; eine anatomische Studie.* 128 pp. Berlin: S. Karger, 1911-1912.
17. Meshberg, P.: An analysis of 128 interposition operations. Am. J. Obst. & Gynec. **21**:398-404, 1931.
18. Pemberton, F. A.: personal communication.
19. Phaneuf, L. E.: The surgical management of prolapse of the uterus and vagina. Surg., Gynec. & Obst. **63**:385-390, 1936.
20. Rongy, A. J.; Tamis, A., and Gordon, H.: Interposition operation for procidentia uteri with a report of 501 cases. Am. J. Obst. & Gynec. **27**:428-439, 1934.
21. Smith, G. V.; Graves, W. P., and Pemberton, F. A.: Procidentia; a study of 683 cases treated between 1875 and 1928 at the Free Hospital for Women, Brookline, Massachusetts. Am. J. Obst. & Gynec. **17**:669-684, 1929.
22. Ward, G. G.: Reconstructive pelvic surgery for genital prolapse: an evaluation of principles. J. Obst. & Gynaec. Brit. Emp. **43**:667-690, 1936.

DISCUSSION

DR. LOUIS E. PHANEUF, Boston: Dr. Fallon in his paper emphasizes the vaginal approach in the treatment of uterine prolapse. It has been my custom to divide prolapse cases into two groups: those women suffering from prolapse who are still young and who are susceptible to future pregnancies, and those afflicted with prolapse who have passed the menopause. In the group of young women the uterus is curetted and a trachelorrhaphy, an anterior colporrhaphy and a perineorrhaphy are performed. The abdomen is then opened, the uterosacral ligaments are shortened and the uterus is suspended. One of three types of suspension is employed, namely the Simpson suspension, the Baldy–Webster suspension or, rarely, the Olshausen suspension, the round ligaments being fixed to the abdominal wall with fine silk. The great majority of patients applying for the relief of prolapse fall in the second group, that is, women who have passed the menopause. In these patients I use the vaginal route entirely, as does Dr. Fallon.

Since no one operation is applicable to all cases of prolapse, I have employed the following methods: interposition operation; vaginal hysterectomy with interposition of the broad ligaments; vaginal hysterectomy (clamp method) and anterior colporrhaphy; high vaginal fixation of the uterus; Fothergill or Manchester operation; and colpectomy, subtotal or total. I have found that each of these methods has its place in properly selected cases. In all cases the perineum is repaired and the cervix amputated if lacerated, hypertrophied or irritated. The cervix is removed in all vaginal hysterectomies.

The interposition operation was described by Thomas J. Watkins, of Chicago, in 1899. Frederick W. Johnson, of the Carney Hospital, adopted it in 1902 and made it the operation of choice in that institution. I have used it somewhat more than any other method, having performed 199 operations. Recurrences have averaged in the vicinity of 10 per cent. A considerable number occurring after ten years were due to extreme atrophy of the uterus, the result having been satisfactory until this took place.

I have not used radium to reduce a large uterus before interposing it, having preferred some other method in the management of this condition. I believe that the interposition operation is contraindicated in the presence of a small atrophied uterus, because the bladder, by its greater weight, will again force out such a uterus.

As Dr. Fallon has pointed out, the interposition operation should not be done before the menopause because of dysmenorrhea and occasionally menorrhagia and metrorrhagia, and because if it is used in young patients fibroids may develop, causing marked difficulties.

Recently, papers have been published from the Johns Hopkins Hospital and the Michael Reese Hospital, of Chicago, emphasizing the advantages of the interposition operation. In the latter institution they have gone back to the interposition operation, after having substituted vaginal hysterectomy for a number of years.

Any operation which conserves the uterus in the treatment of prolapse offers a decided advantage; should recurrence occur it is more easily treated if the uterus has been retained than if it has not.

REPORT ON MEDICAL PROGRESS

CANCER

GRANTLEY W. TAYLOR, M.D.*

BOSTON

THE *American Journal of Cancer* publishes annually about twenty-five hundred abstracts of papers dealing with aspects of malignant disease. The Third International Cancer Congress, held in Atlantic City in September, 1939, offered contributions from approximately five hundred participants. To attempt to summarize this furious activity or to survey as augur the hecatombs of rodents sacrificed in research is not only impossible but unwise. Any presentation must of necessity be superficial and selective.

EXPERIMENTAL CANCER

Chemical Compounds as Carcinogenic Agents

In an excellent review Cook and Kennaway[1] prepared a comprehensive summary of the literature for 1937 on this subject, adding a hundred and eighty new references to their already formidable bibliography. Undoubtedly even more work has been carried out in these fields in 1938 and 1939. Fieser[2] has correlated carcinogenic activity with chemical structure in certain of the aromatic hydrocarbons. While such studies are invaluable to experimental workers, the attempts to transfer the findings to clinical cancer problems are not very successful. Skin cancers occurring in workers with tars and oils, mule spinners' and chimneysweeps' cancers, bladder cancers in aniline workers, the lung cancers in the Joachimsthaler and Schneeberg miners and the osteogenic sarcomas in watch-dial painters are the outstanding examples of cancers due to chemical agents in man.

Hormones

Although the chemical relation of estrogenic hormones to some of the carcinogenic chemical compounds is striking, the attempt to implicate them with carcinogenesis in man has thus far been unsuccessful. Shorr[3] stated: "An analysis of the data leads to the conclusion that no evidence exists that estrogenic hormone, given in physiological doses, has led to the development of carcinoma in man." On the basis of the carcinogenic activity of estrogenic hormone in animals (Lacassagne[4] and others) Gardner[5] believes that the possibility of carcinogenesis by this means in man cannot be dismissed. "There is a great deal of evidence now available," he says, "that any chemical change causing prolonged proliferation of the cells of any type of tissue in the body may act as a carcinogenic agent." This statement obviously refers to the proliferative changes in the breast and female genital tract following administration of estrin.

Viruses

Although viruses play a prominent part in the etiology of a large number of animal neoplasms, they are not considered significant in relation to cancer in man. Andrewes[3] concludes: "There is no proof yet that a virus is concerned in the etiology of cancer in general. But there is evidence to make that idea worth very careful attention."

Genetics

While the geneticists have elaborated their conceptions of the genes responsible for heredity of carcinoma in experimental animals, and have gone so far as to identify two recessive genes, one for malignancy in general and another for organ localization (Slye[6]), Bittner[7] by means of foster-mother nursing experiments has demonstrated that the source of milk exerts a decided influence on the development of breast tumors. Mice nursed by low-tumor-stock females showed a low percentage and mice nursed by high-tumor-stock females had a high ratio of cancer incidence. This finding obviously calls for a revision of a considerable amount of the work on genetics which has been carried out and accepted as proved.

Other Experimental Studies

Andervont,[8] by preliminary implantation of a tumor in a rat's tail, has been able to immunize the animal successfully against later implantation elsewhere in the body (after amputation of the involved tail). This immunity has been carefully studied, but has not yet been explained. Brues[3] has studied growth-inhibiting substances, found in highest concentration in the liver, and in part identified as aliphatic amines. He finds that in vitro they inhibit the growth of normal tissues more readily than that of malignant tissues. Fur-

*Instructor in surgery, Harvard Medical School; assistant visiting surgeon, Massachusetts General Hospital; surgeon, Collis P. Huntington Memorial Hospital, Boston.

ther work on cytotoxins and growth inhibitors promises developments of great interest.

General Considerations

Educational programs designed to reach the public and the general practitioner have been sponsored by the American Society for the Control of Cancer, the American College of Surgeons and numerous other national and state organizations, both in the United States and abroad. These programs differ in detail and in scope, but all are directed toward the achievement of earlier diagnosis and better treatment. Lombard[3] states that "cancer in Massachusetts is in the process of effective control," as shown by "a decrease in delay between the onset of symptoms and visit to physician first noted in 1936; a larger percentage of individuals consulting their physicians in the first month of the disease; an increased use of the tumor diagnosis service; a greater number of individuals with cancer utilizing the clinics; better teaching facilities; an extension of the co-operative cancer control committees; and a steadily decreasing adjusted death rate for females." In spite of this hopeful note, statisticians in general are convinced that cancer is increasing in prevalence, even when due allowance is made for age changes in the population.

Culpability for delay in treatment in a large series of cases was carefully analyzed by Pack and Gallo,[9] and also by Kinney et al.[10]

An important series of studies by Nathanson and Welch[11] on incidence and life expectancy in carcinomas of various regions gives a clear conception of the natural history of the disease. Their curves, properly employed, should make it possible to appraise the efficacy of a method of treatment without the necessity of waiting the conventional five years for a follow-up study (Meigs and Dresser[12]).

Diagnosis

Numerous biological and chemical tests for the presence of cancer continue to be offered by enthusiastic investigators. None of these seem to be of much value. Pfeiffer and Miley[3] attempt to show specific alterations in the crystallization form of copper chloride when serum of a cancerous individual is added to the solution. They claim 80 per cent of positive tests in cancer cases, and 10 per cent of false positives in control cases.

Refinements in roentgenology have accounted for considerable improvement in cancer diagnosis, but they are too numerous to recapitulate here. Endoscopy, notably gastroscopy and peritoneoscopy, has improved the diagnosis in numerous cases. Aspiration biopsy (Martin and Ellis[13]) has many supporters. Opponents point out the possibility of dissemination by this procedure. It is also emphasized that the amount of tissue secured is often inadequate even in the hands of expert pathologists. McLean and Sugiura[14] carried out aspiration biopsies repeatedly on transplanted rat and mouse sarcomas without increasing the percentage of distant metastases.

Treatment in General

Effective cancer therapy is still restricted to surgery, radium and x-ray. Improvements in surgery are chiefly technical, and deal with malignancies in special fields. The introduction of electrosurgery several years ago marked a distinct advance in the operation management of certain types of carcinoma. More recently the introduction of two active electrodes held close together has further improved this method of treatment. Improvements in anesthesia and in maintaining the patient's physiologic equilibrium have widened the scope of surgery and diminished its mortality. The use of zinc peroxide (Meleney,[15] Sunderland and Binkley[3]) has made it easier to clean up foul and sloughing ulcerations.

However brilliant may be the technical advances in surgery, this method of treatment can be applied to malignancy only in an early and localized stage of the disease. Thus improvement in results of surgery, especially as concerns the total cancer problem of an anatomic region, must depend primarily on an educational program which will help to discover a greater proportion of the cancer cases in a stage favorable for cure.

A similar limitation of radical therapeutic effort to early and favorable cases does not apply to radiation therapy. Thus, advances in technology in this field carry the possibility of their application to a large proportion of the sufferers from a given type of cancer, including late neglected patients as well as those with early localized lesions.

Radiation therapy was recently reviewed in this journal by Dresser.[16] The biology of roentgen therapy is still under investigation. Guyer and Claus[3] and others have experimentally administered colchicine to animals before radiation in order to arrest cell division in the metaphase. They found that irradiation applied to the tumors was made more effective by this means. The attempt to adjust radiation dosage and intervals to the biology of the malignant cell probably accounts for the efficacy of the Coutard technic of radiation, as opposed to the single massive dose. Similar benefits also inhere in the Chaoul method of fractionated contact irradiation, as well as Pfahler's so-called saturation technic. The role of supervoltages in treatment is still under review. X-ray therapy

seems to be supplanting radium in some fields; and platinum filtered radium needles have supplanted the use of radon seeds in many cases in which interstitial radium is employed. The use of radioactive isotopes (Lawrence[3]) is still a purely experimental field but one which is of great interest.

Laborde,[17] writing on the subject of acquired radio-resistance, points out that the effect of radiation is on the host tissues rather than on the tumor itself. Hence resistance develops as the host tissues undergo changes in the vascular bed and fibrosis supervenes.

There have been reported some cases of pathologic fracture of the femoral neck following x-ray therapy which involved the pelvis, and one such case has been observed at the Pondville Hospital. Numerous writers have reported studies of the pulmonary fibrosis which may follow roentgen therapy of the chest.

Smith and Fay[18] have recently demonstrated the beneficial effect of local and general refrigeration as a palliative procedure. This work continues to be experimental, and will apparently require extensive physiological and clinical study before its efficacy can be determined. Other methods of pain control — sedatives, narcotics, neurosurgical measures and alcohol injections — have been effective in the vast majority of cases. Favorable reports have been made on the use of cobra venom for the relief of pain.

Regional Carcinoma

References to advances in the treatment of cancer of special regions have already appeared in this journal, and no attempt will be made to cover the entire field. A few developments appear to be of special interest and will be recorded.

Cancer of the Mouth

Erf and Rhoads[3] and Martin[3] have made a careful study of vitamin B deficiency as it relates to precancerous and cancerous changes in the oral mucosa. Franseen[19] has studied the Plummer-Vinson syndrome as a precancerous condition presumably due to deficiency disease. Nathanson and Weisberger[20] have carried out therapy with estrogens in cases of oral leukoplakia, with considerable benefit. It is likely that these vitamin- or hormone-deficient states provide a favorable ground on which the chronic irritation of bad teeth and tobacco can excite cancerous changes. The high incidence of multiple oral cancers (Lund[21]) is in favor of such a theory.

Berven[22] and Martin[23] both report excellent results on unselected series of mouth cancers by the use of intensive radiation therapy, with cures of 25 and 26 per cent respectively. Management of the cervical lymph nodes is by means of watchful waiting, surgery in selected cases and usually radiation as well. Duffy[24] has formulated the indications for cervical lymph-node dissection, and reports about 20 per cent cures in those cases with involved nodes which are subjected to radical dissection. Carcinoma of the lip has a much better prognosis, and is curable by neck dissection in nearly 60 per cent of patients who are subjected to operation with cervical node metastases (Taylor and Nathanson[25]). Unfortunately, in both lip and mouth carcinoma many patients first present themselves with carcinomatous metastases which are already inoperable. In these cases radiation as advocated by Martin will occasionally effect a cure. Surgery following intensive radiation is extremely hazardous, as Dresser[16] has pointed out.

Thyroid Gland

In no field is the pathologist confronted with greater difficulty than when trying to correlate the histologic picture with the clinical course in thyroid malignancy. Vein invasion, histologically a malignant characteristic, is frequently a benign clinical condition. The presence of aberrant thyroid tissue and its tendency to malignant change are also confusing. In addition there is the likelihood of late recurrence, even after apparent cure has been effected. In general, treatment is by radical surgery combined with intensive radiation therapy. Ward[3] reported cures in 30 per cent of a series of 95 cases subjected to operation.

An interesting epidemiological finding is the geographic relation between goiter and cancer in general (McLendon[26]). This conclusion has been substantiated by other authors. There is no very satisfactory explanation of this correlation.

Larynx

Surgery, in the opinion of certain operators, continues to be the treatment of choice in small, localized growths in the larynx; however, the excellent results secured with radiation without mutilation seem to be an improvement on the results that can be secured by surgery.

Esophagus

Carcinoma of the esophagus is well-nigh hopeless so far as cure is concerned. An increasing number of attempts at surgical extirpation are being carried out, and the field remains a challenge to the surgical virtuoso. Radiation has been disappointing in general as a cure, although technical advances may improve the results. Excellent palliation is often secured by radiation. Bougienage is a hazardous procedure and of only ephemeral benefit. Fanciful and elaborate gas-

trostomies are devised, but they involve a considerable mortality and do not greatly prolong the life of the patient.

Lung

There seems to be universal agreement that carcinoma of the lung is increasing. Ochsner[3] insists that total pneumonectomy should be carried out in all operable cases, in order that a few lymph nodes may be removed. In the pathologic material which he analyzed 83 per cent of the cases presented regional node involvement. He also reported a mortality following pneumonectomy of 50 to 60 per cent. Since pathological confirmation of lung tumors is not usually available preoperatively, it seems unwise to advocate total pneumonectomy as a routine procedure.

Superior sulcus (Pancoast) tumors appear not to be a pathological entity. The syndrome associated with them is produced by the anatomic location.

Breast

Keynes[27] retains his interest in interstitial radium treatment of carcinoma of the breast, and results in his hands compare favorably with those secured by surgery. Recent sporadic impulses toward simple mastectomy in selected cases are retrogressive. The fallibility of clinical appraisal of axillary lymph-node involvement is sufficient argument to urge against the occasional efficacy of this method of treatment. Cures can be effected in 70 to 75 per cent of cases without axillary involvement, and in 25 to 30 per cent of cases with axillary involvement, by radical surgery alone (Simmons, Taylor and Welch[28]), provided cases are properly selected. The arguments for preoperative or postoperative radiation are unconvincing.

Stomach

Balfour,[29] reporting the Mayo Clinic experience with carcinoma of the stomach, gives a radical operability of 45 per cent, with an operative mortality of 14 per cent. Cures were effected in 48 per cent of the patients without lymph-node involvement and in 18 per cent in cases which had node metastases. These figures are more favorable than those secured by other surgeons. Total gastrectomy continues to be carried out in an increasing number of cases and perhaps an occasional cure may result. Lahey[3] has recently reemphasized the value of copious preoperative gastric lavage with dilute solutions of hydrochloric acid.

Colon and Rectum

Allen[30] recently commented on the excellent results reported in these fields by the use of Devine's method of preliminary colostomy. In general there seems to be increasing enthusiasm for two-stage radical operations on the colon. According to Dixon,[3] the operability in colonic lesions is fairly high (71 per cent), the operative mortality in experienced hands is diminishing (20 per cent) and gross curability is fairly satisfactory (33 per cent).

The one-stage radical operation of the Miles type has become the method of choice for carcinoma of the rectum, with an operability of from 57 (Jones[3]) to 75 (Rankin[3]) per cent, an operative mortality of 7 per cent (both authors) and cures in the neighborhood of 56 per cent (Jones). Electrosurgical methods have been urged as a palliative procedure in inoperable rectal growths, without finding many enthusiastic supporters. Radiation is occasionally urged for these cases but has not proved helpful in most clinics. Studies on the spread of rectal cancer have been made by Gordon-Watson[31] and Bacon and Gilbert.[32]

Cervix

Schiller's test with iodine is now widely used to help detect suspicious areas in the uterine cervix, and an occasional early cancer may be discovered by this means. Colposcopy (Hinselmann) calls for great experience in interpretation of the appearances observed and has not achieved much popularity. Treatment seems to be tending toward standardization, with combined external roentgen therapy and intracavitary radium application. Divided and sustained radiation dosage seems to be better than single massive treatments. A few authors continue to advocate radical surgery in selected early cases.

The apparent relatively infrequent occurrence of carcinoma of the cervix in Jewesses is very interesting and calls for searching investigation (Auster[3]).

Functioning Adenomas

Great interest is shown in functioning adenomas of the ductless glands. The cases in general are rare, the syndromes are striking and results of surgical treatment are brilliant. Sometimes these tumors develop malignant characteristics, with death due to regional or generalized metastases. Studies of these patients shed more light on the functions of the ductless glands than on the etiology of cancer.

264 Beacon Street.

REFERENCES

1. Cook, J. W., and Kennaway, E. L.: Chemical compounds as carcinogenic agents; first supplementary report: literature of 1937. Am. J. Cancer **33:**50-97, 1938.
2. Fieser, L. F.: Carcinogenic activity, structure, and chemical reactivity of polynuclear aromatic hydrocarbons. Am. J. Cancer **34:**37-124, 1938.
3. Andrewes, C. H.; Auster, L. S.; Brues, A. M.; Dixon, C. F.; Erf, L. A., and Rhoads, C. P.; Guyer, M. F., and Claus, P. E.; Jones, T. E.; Lahey, F. H.; Lawrence, J. H.; Lombard, H. L.; Martin, C. L.; Ochsner, A.; Pfeiffer, E. E. L., and Miley, G. P.; Rankin, F. W.; Shorr, E.; Sunderland, D., and Binkley, J. S.; and Ward, R.: papers read at the Third International Cancer Congress, Atlantic City, New Jersey, September 11-15, 1939. Abstracts were published in the program, and the papers will appear in full in the *Transactions*.
4. Lacassagne, A.: Statistique des différents cancers constatés dans les lignées sélectionnées de souris, après action prolongée d'hormones oestrogènes. Bull. Assoc. franç. p. l'étude du cancer **27:**96-116, 1938.
5. Gardner, W. U.: Estrogens in carcinogenesis. Arch. Path. **27:**138-170, 1939.
6. Slye, M.: L'hérédité dans le cancer. Bull. Assoc. franç. p. l'étude du cancer **26:**138-153, 1937.
7. Bittner, J. J.: Relation of nursing to extra-chromosomal theory of breast cancer in mice. Am. J. Cancer **35:**90-97, 1939.
8. Andervont, H. B.: Studies on immunity induced by mouse sarcoma 180. Pub. Health Rep. **47:**1859-1877, 1932.
9. Pack, G. T., and Gallo, J. S.: Culpability for delay in treatment of cancer. Am. J. Cancer **33:**443-462, 1938.
10. Kinney, K. K., et al.: Symposium presented at tenth meeting of Association of Connecticut Tumor Clinics. J. Conn. M. Soc. **3:**118-120, 1939.
11. Nathanson, I. T., and Welch, C. E.: Life expectancy and incidence of malignant disease. I. Carcinoma of breast. Am. J. Cancer **28:**40-53, 1936. II. Carcinoma of lip, oral cavity, larynx and antrum. *Ibid.* **31:**238-252, 1937. III. Carcinoma of gastro-intestinal tract. *Ibid.* **31:**457-466, 1937. IV. Carcinoma of genito-urinary tract. *Ibid.* **31:**586-597, 1937. V. Malignant lymphoma, fibrosarcoma, malignant melanoma, and osteogenic sarcoma. *Ibid.* **31:**598-608, 1937.
12. Meigs, J. W., and Dresser, R.: Carcinoma of cervix treated by roentgen ray and radium. Ann. Surg. **106:**653-667, 1937.
13. Martin, H. E., and Ellis, E. B.: Biopsy by needle puncture and aspiration. Ann. Surg. **92:**169-181, 1930.
14. McLean, J., and Sugiura, K.: Does aspiration biopsy of tumors cause distant metastasis? J. Lab. & Clin. Med. **22:**1254-1257, 1937.
15. Meleney, F. L.: Prophylactic and active use of zinc peroxide in foul smelling mouth and neck infections. Ann. Surg. **107:**32-38, 1938.
16. Dresser, R.: Radiation therapy. New Eng. J. Med. **221:**386-388, 1939.
17. Laborde, S.: Zur Frage der erworbenen Radioresistenz bei Epithelgeschwülsten. Strahlentherapie **56:**466-477, 1936.
18. Smith, L. W., and Fay, T.: Temperature factors in cancer and embryonal cell growth. J. A. M. A. **113:**653-660, 1939.
19. Franseen, C. C.: unpublished data.
20. Nathanson, I. T., and Weisberger, D.: The treatment of leukoplakia buccalis and related lesions with estrogenic hormone. New Eng. J. Med. **221:**556-560, 1939.
21. Lund, C. C.: Second primary cancer in cases of cancer of buccal mucosa; mathematical study of susceptibility to cancer. New Eng. J. Med. **209:**1144-1152, 1933.
22. Berven, E. G. E.: Radiological treatment of malignant tumours of oral cavity and pharynx. Acta radiol. **18:**16-30, 1937.
23. Martin, H.: Intra-oral cancer. Yale J. Biol. & Med. **8:**652, 1936.
24. Duffy, J. J.: Cervical lymph nodes in intraoral carcinoma: surgery or irradiation? Am. J. Roentgenol. **39:**767-777, 1938.
25. Taylor, G. W., and Nathanson, I. T.: Evaluation of neck dissection in carcinoma of the lip. Surg., Gynec. & Obst. **69:**484-492, 1939.
26. McLendon, J. F.: Statistical relation between goitre and cancer. Am. J. Cancer **35:**554-558, 1939.
27. Keynes, G.: Conservative treatment of cancer of the breast. Brit. M. J. **2:**643-647, 1937.
28. Simmons, C. C.; Taylor, G. W., and Welch, C. E.: Carcinoma of the breast. Surg., Gynec. & Obst. **69:**171-177, 1939.
29. Balfour, D. C.: Factors of significance in prognosis of cancer of stomach. Ann. Surg. **105:**733-740, 1937.
30. Allen, A. W.: Abdominal surgery. New Eng. J. Med. **220:**290-296, 1939.
31. Gordon-Watson, C.: Origin and spread of cancer of rectum in relation to surgical treatment. Lancet **1:**239-245, 1938.
32. Bacon, H. E., and Gilbert, P. D.: Sites of metastases from carcinoma of anus, rectum and sigmoid colon. J. A. M. A. **111:**219-221, 1938.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25461

PRESENTATION OF CASE

A forty-two-year-old American chemist was admitted to the surgical service complaining of stomach trouble.

For five years before admission the patient had had attacks of abdominal pain accompanied by nausea, vomiting and occasionally diarrhea. These attacks first came at intervals of about six to eight months, and usually lasted from a few days to a few weeks, but they gradually became more frequent, and starting fourteen months before entry, they occurred once a month. These attacks had characteristically followed a definite course. Generally there was a premonitory phase of two or three days during which time the patient suffered from general malaise, marked anorexia and mild "gas pains." Following these early mild symptoms, lower abdominal, cyclic, steadily progressive, severe, cramping "gas pains" occurred every fifteen to twenty minutes. As the attacks persisted, the pains tended to become almost continuous and were then associated with nausea and vomiting. The latter usually brought relief. On some occasions an intestinal pattern was observed on the abdominal wall with the passage or "gurgle" of gas; this frequently disappeared, at which time the pains would cease. Often morphine and atropine hypodermically were required for relief. Profuse diarrhea usually followed these attacks. They were precipitated by eating foods with a high residue. Once the premonitory symptoms had appeared, however, the episodes could be aborted by a regime of mineral oil and a liquid diet. The last severe attacks occurred nine and eighteen months before admission. On these occasions there were no premonitory symptoms; the attacks were ushered in by chills, a rapid pulse, a temperature rise and sweating. The stools were never clay colored, tarry or bloody. There had been a weight loss of several pounds.

The patient was born and had lived most of his life in Massachusetts. Nineteen years before admission he had had influenza, which was followed by pleurisy, pneumonia and a cough said to be due to "chronic bronchitis." This cough with sputum continued for two years. At this time while running to catch a train he coughed up large quantities of blood. A diagnosis of pulmonary tuberculosis was made, and he was sent to a sanatorium where he remained for four years. His sputum was positive for tubercle bacilli at entry but soon became negative and remained so for his whole hospital stay; he was discharged thirteen years before the present entry. He seemed well until nine years before admission when he had another small hemoptysis. He sought no hospital treatment. One and a half years before admission the patient's sputum became positive. He was told that he had bilateral chronic fibroid tuberculosis with one or two small cavities; he entered another sanatorium where he remained until three months before entry. His gastrointestinal complaints were investigated while he was hospitalized. Two gastrointestinal series were done one year before admission, and both were described as negative. He entered here for further studies, for he thought that his gastrointestinal symptoms were not functional, as they had been described to him.

The physical examination revealed a poorly developed, undernourished man. There was dullness at both pulmonary apices, with bronchial breathing but no rales. Expansion was equal. Examination of the heart was negative. A freely movable tumor was palpated in the right lower quadrant. The rectal examination was negative.

The temperature, pulse and respirations were normal.

Examination of the urine was negative. Blood examination showed a red-cell count of 4,600,000 with 80 per cent hemoglobin (Sahli), and a white-cell count of 11,000. Four sputum examinations were negative for acid-fast organisms. The serum protein was 6.2 gm. per 100 cc.

Roentgenographic studies showed the ileum to be markedly dilated. It appeared that the entire cecum and a portion of the terminal ileum were intussuscepted into the ascending colon. A barium enema passed to the cecum without delay. The cecum was blunt and appeared shortened, and there was a filling defect at its tip about 4 cm. in diameter. The tip of the cecum was opposite the crest of the ilium, and it was not possible to fill the terminal ileum, which was dilated and contained gas.

On the second hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ARTHUR W. ALLEN: May we see the x-rays?

DR. GEORGE W. HOLMES: We have a series of x-ray films taken in the usual manner, some with the colon filled and others with it empty, and still others taken during fluoroscopic observation, the so-called spot films. There are one or two striking things in these films. First, as described

in the text, the cecum itself is never well filled. Secondly, there is some definite dilatation of the terminal ileum. Thirdly, there is this large filling defect in the cecum, which from our observations is quite characteristic of herniation of the ileum into the cecum. It changes a good deal in successive films: sometimes it is quite large, at other times small. A solid tumor within the cecum would not do that. It has to be a mass which moves in and out of the cecum. Then the brilliancy shows that it contains a considerable amount of gas. In some of the films, you can see a lobulated round mass within the ileum, about the size and shape of a walnut, and there is no question it is in the ileum, not the cecum. We should interpret the finding then as a mass in the terminal ileum which produced a certain amount of obstruction and caused the ileum to be herniated into the cecum.

Dr. Allen: Without any question we have a man who had pulmonary tuberculosis. He also had an abdominal condition which had caused him a good deal of trouble in the five years prior to admission, and I suppose the first thing we should think about is tuberculosis of the cecum. On the other hand, Dr. Langdon Parsons has studied our cases of tuberculosis of the cecum and found a number of such patients who did not have tuberculosis elsewhere and who had no evidence of pulmonary tuberculosis. We might, in other words, get one without the other. This man's story of recurring attacks of pain over a long period of time, not varying particularly in intensity until eighteen months prior to admission, might indicate that the condition had changed during the past year and a half. Symptoms had been produced over a period of three and a half years by a high residue diet and relieved by a liquid diet plus mineral oil. This reminds us of a good many functional disorders that we have seen causing mild intestinal obstruction and brought on by a high roughage diet. A good example is seen occasionally in the diabetic patient who uses an excess of bran in his diet. In the South they have cases of intestinal obstruction from the residue formed from persimmons. This fruit grows wild and is considered to be delectable in season. The persimmon bezoar has become a well-known entity in certain districts. These may pass the pylorus and produce intestinal obstruction. Several years ago we explored a man here for acute intestinal obstruction and found that 60 or 90 cm. of the terminal ileum was packed with corn which he had obviously not masticated too well. In the hospital now there is a boy who has been operated on three times for small-bowel obstruction. At the last operation it was found that the obstruction was due to a large quantity of apple pulp that the boy had not chewed well. So we can get intestinal obstruction from roughage alone. However, the other causes of recurrent attacks of obstruction have to be considered. Recurring intussusception is a very common one. We are told that this man may have had an intussusception, a statement which makes me a bit suspicious, but it is possible to have recurring intussusceptions at quite infrequent intervals, which are usually due to some tumor in the neighborhood of the ileocecal valve. I think Dr. Richard Schatzki has collected the intussusception cases in this hospital and reported some 18 or 20 cases in adults. He found that approximately half of them were on a benign basis, such as a benign lipoma in the wall of the large bowel or a polyp in the region of the ileocecal valve. Why Dr. Holmes called my attention to the tumor in the terminal ileum, I am not sure. It bothers me a little but must be considered. We also occasionally see cases of torsion of the cecum, a volvulus that produces temporary obstruction with spontaneous release.

One of course must always think of the possibility of recurring appendicitis in considering cases with repeated attacks of abdominal pain. It is difficult to account for the picture on this basis, however, because his symptoms had been so clearly mechanical until eighteen months prior to admission. The last two attacks were quite different. In these he had no premonitory phase. These attacks were ushered in by chills, a rapid pulse, fever and sweating. He insisted that his stools were never changed in character, so far as being clay colored or tarry, and we have no history of diarrhea except after his earlier bouts of obstruction. The onset of abdominal pain and chills interests me a good deal because we studied the cases of postappendiceal pylephlebitis that had occurred in this hospital and found that in every instance the initial attack of appendicitis had been started with a chill. We found, however, that about 6 per cent of all cases of acute appendicitis started with chills. Inasmuch as the ratio of pylephlebitis to acute appendicitis was only 1 to every 300 cases, it means that a good many cases of acute appendicitis may start with chills without developing pylephlebitis.

We must think also, in relation to the chills and a palpable mass in the right lower quadrant, of the fact that when carcinoma of the colon metastasizes to the liver, there is very apt to be a general reaction and chill. Occasionally one can date the time of liver involvement by that symptom. Also, one would have to consider an abscess that had occurred and drained itself.

This man had no anemia. His blood was within

normal limits but that does not of itself rule out cancer of the right bowel, although we are more apt to see anemia associated with cancer of the right colon than we are with cancer of the left. However, we do see quite extensive lesions with no anemia. A slight leukocytosis does not tell us one thing or another. We should like to have known what his stools were like after admission to the hospital, and whether they were guaiac positive; but the record does not tell us that.

The question then comes down to differential diagnosis. We have a man with pulmonary tuberculosis, recurrent attacks of abdominal pain and a palpable tumor in the right lower quadrant. We have to consider a certain number of possibilities. Dr. J. H. Means has pointed out that lymphoma must be considered in every case of differential diagnosis of tumor within the abdomen. I should expect if this were lymphoma that this mass would not have been so freely movable. I should expect that there would not have been this long history of five years, provided we can connect the early attacks with the later attacks. One must, of course, consider regional ileitis, a disease that may manifest itself over a long period of years and produce quite peculiar symptoms. One must also consider tuberculosis of the cecum, and I have considered it quite seriously. I very much doubt that this man had tuberculosis of the bowel; his symptoms have been too intermittent, and the tuberculous cecums that I have happened to see have not been so freely movable on palpation as this one was. One must, of course, consider recurring acute appendicitis with abscess formation, but it would be a very unusual form of appendicitis and I do not expect that it will prove to be that. Could a Meckel's diverticulum produce a situation in this region that would allow intussusception into the cecum? Dr. Holmes points out that this little affair here looks quite like a Meckel's diverticulum as seen on a film, but one wonders how far this projection really is from the cecum and whether enough of the terminal ileum has been intussuscepted into the right colon to allow one to toy with the idea that it might be a Meckel's diverticulum. I wondered if it could be a polyp with a long stalk. I think it is not a polyp since the barium apparently outlines the inner side of it. A benign tumor in this region of course must be taken into consideration and that I believe is the commonest cause of chronic intussusception in the adult. Carcinoma in this region must be considered also, but I believe that this lesion was probably not malignant — at least it is fair to say that it could not have been malignant for five years and still have been as freely movable as it appeared to be at the time of entry.

So I come down to hazarding a guess that this was a benign tumor of the terminal ileum, that it had for some reason or other produced chronic recurring attacks of intussusception, and that its exact nature would be impossible to determine until after operation.

DR. TRACY B. MALLORY: Have you anything to say, Dr. Holmes?

DR. HOLMES: The question of Meckel's diverticulum was raised. I did not believe it was that. The general opinion in the X-ray Department was that it was a tumor in the wall of the ileum. We did not go any farther.

DR. MALLORY: Dr. Homans, have you ever seen an area of regional ileitis intussuscept into the cecum?

DR. JOHN HOMANS: I cannot conceive of it because of the stiffness of the wall of the bowel. I have an impression that some infection played a role here, perhaps superimposed on the original tumor. It might even have been an appendicitis of a sclerosing sort.

DR. CHESTER M. JONES: Hyperplastic tuberculosis can give recurring attacks of obstruction with no intervening symptoms for intervals of many, many months, I believe. I do not know whether it would assume a form of tumor like this. I am somewhat inclined to doubt it, but I think this might be hyperplastic tuberculosis in one of its rare forms. One form of obstruction Dr. Allen did not include is that caused by ascaris.

DR. ERNEST M. DALAND: In going over this man's story we found that he had had pulmonary tuberculosis with apparent arrest of the tuberculosis from institutional care. He had not felt well for about seven years and had been unable to work more than a day or two at a time. He had been back to the sanatorium, and they believed that he did not have enough in the chest to make him feel as badly as he did. While there the last time he had several of these attacks, but they usually came on after five o'clock in the afternoon or early in the morning. Many times he asked to have the house doctor come to see him in an attack, but by the time he was seen in the morning the symptoms had cleared up. There was that one important point — he had something that did not seem to be explained by pulmonary tuberculosis. This man went to the Baker Memorial Hospital for x-ray studies. The afternoon after the films were taken I saw him at my office, together with the x-ray report. At that time his symptoms had entirely cleared up, but it was suggested that he go immediately into the hospital. He waited three days, and when he entered, was

entirely free from symptoms. So we know that he had a recurring intussusception that did entirely clear up between the attacks.

He was operated on under spinal anesthesia, and nothing was found except in the region of the cecum and the terminal ileum. The terminal ileum was very much thickened and dilated. About 12 cm. from the ileocecal valve was a circular ridge of lesions which we decided were tuberculous. The cecum was entirely replaced by a very large hard mass, much harder than we had suspected before operation. We were certain that the lesion was tuberculous, but whether or not there was a superimposed carcinoma we could not say. A lymph node was removed for diagnosis, and an anastomosis was done between the terminal ileum and the transverse colon.

He made a very good recovery, except for a good deal of cough following operation. Thirteen days later a second operation was done, and the right colon was removed. At that time the pathological diagnosis of tuberculosis of the lymph node had been made, but even then we were not sure that we were not dealing with two processes. A right colectomy was done. He made a very good convalescence and left the hospital free from symptoms. His appetite came back; he returned to work as a chemist, has worked ever since, has gained weight and has been in good health.

Preoperative Diagnoses

Carcinoma of cecum?
Tuberculosis of cecum?
Recurring intussusception.

Dr. Allen's Diagnoses

Benign tumor of the ileum, with recurring intussusception.
Pulmonary tuberculosis.

Anatomical Diagnoses

Tuberculosis (hyperplastic type) of the ileum and cecum.

Pathological Discussion

Dr. Tracy B. Mallory: The specimen which came to the laboratory showed multiple areas of involvement with tuberculosis. The lesions were definitely nodular in type, with comparatively little ulceration, and may, I believe, be classified as so-called "hyperplastic tuberculosis." Several of them were clustered right about the ileocecal valve, and one nodule was 5 or 6 cm. up the ileum. There was one small area of involvement in the cecum, but the major disease was in the ileum rather than in the cecum. I presume that the tumor which Dr. Holmes described in the ileum was the upper, rather isolated nodule.

We used to think of intussusception as something that was virtually an act of God, perhaps that rather malign deity whom the insurance companies so frequently invoke, but in recent years, in adults at any rate, we have found that almost invariably the intussusception can be explained on the basis of some chronic underlying factor, which in our experience has most frequently proved to be benign tumor, as Dr. Allen pointed out.

CASE 25462

Presentation of Case

First Admission. A sixty-three-year-old Irish housewife was admitted to the medical service complaining of occipital headaches.

The patient regarded herself as well until seven and a half months before admission when she accidentally fell, struck the back of her head and lower spine and was unconscious for three hours. She remained in bed for the following two weeks, complaining of soreness and transient pain in the lower back. There was no retrograde amnesia or subsequent loss of consciousness. Six and a half months before entry she began to have headaches and profuse nosebleeds. The former were chiefly occipital but were also referred to the top of the head and the temples. They occurred with increasing frequency and intensity, becoming daily, usually in the evening. The nosebleeds were profuse, occurred several times weekly and characteristically seemed to relieve the dull aching fullness in the occipital region. During the six months before admission the patient had almost constant nausea but did not vomit, except on a few occasions when she raised swallowed nasal blood. The nausea resulted in anorexia so that she ate sparingly and lost 17 pounds in weight. During the present illness she had noted the gradual appearance of telangiectatic veins on her cheeks.

About five weeks before entry the patient developed an acute respiratory infection characterized by right chest pain, cough with rusty sputum, malaise, several chills and a temperature of 103°F. These symptoms subsided over a period of two weeks, but she did not regain her accustomed strength and as a result spent most of her time abed. She felt "feverish" evenings, and when seen in the Out Patient Department ten days before admission her temperature was 99.4°F. While kneeling to say her prayers nine days before entry she fell against her bed and received a black eye and a bruised shoulder. These subsided rapidly.

For four or five years she had had a sallow or "bilious" complexion as often as once a month, but no frank jaundice. The stools and urine were normal, and there was no pruritus. The patient had been married forty-five years and had had thirteen children, nine of whom were living and well. She had had seven miscarriages.

Physical examination revealed a well-developed and moderately obese woman who had a florid complexion and a protuberant abdomen. There were telangiectases along the sides of the nose and over the cheeks. The tongue was deep red but not smooth. The veins of the optic fundi were engorged, but the disks were normal and there were no pulsations in the vessels. There was a moderate kyphosis in the dorsal spine. The heart was not enlarged. There was a soft non-transmitted systolic murmur heard at the apex. Examination of the abdomen revealed a smooth, firm, non-tender, liver edge four fingerbreadths below the costal margin, with questionable shifting dullness in the flanks. An otherwise negative neurological examination showed a cogwheel rigidity in both arms, with a tendency to a slow, slight tremor in the arms and legs. The blood pressure was 150 systolic, 80 diastolic.

The temperature, pulse and respirations were normal.

Examination of the blood revealed a red-cell count of 4,860,000 with a hemoglobin of 111 per cent, a cell volume of 48.5 per cent, a volume index of 1.20 and a color index of 1.11; the white-cell count was 10,000 with 45 per cent polymorphonuclears. The specific gravity of the urine was never higher than 1.012. The stools were brown, formed and guaiac negative. A blood Hinton test was positive, a Wassermann test negative. A qualitative test for follicle-stimulating hormone in the urine was positive. Two bromsulfalein liver-function tests showed 45 and 35 per cent dye retention. The serum nonprotein nitrogen was 16 mg. per 100 cc., and the van den Bergh biphasic and slightly above normal. The Takata-Ara and formol-gel tests were strongly positive. A capillary blood-sugar tolerance curve read as follows: fasting 105 mg., one-half hour 156 mg., one hour and five minutes 178 mg., two hours 176 mg., three hours 144 mg. and four hours 117 mg. per 100 cc. X-ray studies of the esophagus, stomach, duodenum, chest and skull were negative. There was no enlargement of the liver. Intravenous pyelograms showed no evidence of disease in the upper urinary tract. Multiple diverticula in the transverse and descending colon were shown by barium enema.

The patient ran an uneventful hospital course with normal temperature, pulse and respirations throughout. She tired of the numerous studies done on her and was discharged on the eighteenth hospital day with her work-up incomplete and her disease undiagnosed.

Final Admission (seven months later). A supplementary history obtained from the family physician revealed that the patient had drunk about 3 oz. of whisky daily for six years. A few days after her hospital discharge she was given two injections of neoarsphenamine by her physician. These were followed by chilly sensations, fever and malaise, without urticaria or bronchospasm. Three weeks later she developed jaundice after the third of six weekly bismuth injections. Four months before admission a three-week period of jaundice with "gall-bladder colic" appeared. Her physician stated that she had received no cinchophen, phenacetin or amidopyrine. From six weeks before admission until entry the patient became increasingly jaundiced. Her urine became the color of molasses, and her stools clay colored. Two weeks before entry her ankles and abdomen became swollen.

Physical examination was identical with that of the first admission, except that she was more undernourished, lethargic and deeply jaundiced, with numerous scratch marks and many telangiectases on the skin. The abdomen was protuberant and contained striae. Shifting dullness was present. The liver and spleen were not felt.

The temperature was 99.6°F., the pulse 100, and the respirations 35.

The red-cell count was 3,100,000 with 84 per cent hemoglobin, and the white-cell count 9900 with 77 per cent polymorphonuclears. The clotting time was ten minutes, the bleeding time three minutes (cuff and stab method). The urine examination showed a specific gravity of 1.018, with a +++ albumin, a ++++ bile and a negative sediment. The stools were brown and formed. The serum van den Bergh was 23.6 mg. per 100 cc., direct. A bromsulfalein test showed 95 per cent retention; the total serum protein was 7.6 gm. per 100 cc., the total cholesterol 49 mg.

The patient ran a steady, gradually downhill course; she became apathetic, then stuporous and on the fifth hospital day comatose and incontinent. She died on the seventh hospital day.

Differential Diagnosis

Dr. Thomas V. Urmy: This is a rather complicated case with several unusual features, particularly in the laboratory tests. I think that we shall make most rapid progress by attacking first the most prominent part of the picture—the very apparent disease of the liver. If we take the second entry alone, we have the typical picture of a failing liver, with an early exitus.

Going back over the history of the first admission we find that there are a number of facts which may be significant. In the first paragraph there is a statement that the patient had constant nausea for about six months before admission. We should be much more willing to ascribe nausea without vomiting to liver disease than to the reported head injury. There is also a note of telangiectatic veins in the cheeks. Then she acquired an acute respiratory infection, apparently pneumonia, following which she was less well and continued to run a low-grade fever for some time. It is very common in cirrhosis of the liver to see some intercurrent infection, even a mild one, greatly activate the hepatic process; fever may persist for several weeks. We therefore have every reason to suspect that she was suffering from cirrhosis which had been relatively asymptomatic until the pulmonary infection.

Physical examination the first time showed telangiectases, and the red tongue, not smooth, which is very often found in cirrhosis and is probably due to general nutritional deficiency. The liver was enlarged, and there was some question of ascites. Going on to the laboratory tests we find a high normal red-cell count for a woman, a very high hemoglobin and an elevated cell volume, color index and volume index. In cirrhosis of the liver it is not uncommon to get this type of blood, with the exception that there is almost always an anemia. I cannot explain the absence of the latter, but it is very unlikely that she had an Addison's anemia. The bromsulfalein test gives further evidence of liver disease; retentions of 45 and 35 per cent are consistent with cirrhosis. The serum nonprotein nitrogen was normal. The van den Bergh was not significantly elevated, but such a finding is not inconsistent with the diagnosis of cirrhosis. The positive Takata-Ara and formol-gel tests are strong evidence in its favor. The blood-sugar tolerance test I cannot explain entirely. It was prolonged, as you would expect in a diabetic, and this raises the question of hemachromatosis. However, there was no further evidence of this disease. It may be that damaged liver function, with reduced capacity of absorbing glucose, was responsible for the prolonged curve, although I do not see why the fasting sugar should have been so high. The x-ray studies do not help. The esophagus apparently showed no varices, although we do not know whether they were looked for. No enlargement of the liver was noted, although apparently it was easily felt on physical examination. I doubt if the liver had shrunk very much between the physical and x-ray examinations. The patient had a normal temperature in the hospital.

On the final admission we have much more evidence pointing to liver disease, all of which is consistent with failing cirrhosis. Two toxic agents are mentioned. She had been drinking whisky daily, and she also had received neoarsphenamine, several weeks after which she developed jaundice. We know that two weeks before entry the ankles became swollen and the abdomen larger. At entry she showed lethargy, deep jaundice, apparent increase in the size of the abdomen, and shifting dullness, all of which are typical of liver failure in portal cirrhosis. The liver was not felt this time, which is consistent with shrinkage in size. The fact that the spleen was not felt is not necessarily significant. At this time the red count was lower than at the first admission, which is consistent with cirrhosis. The color index was still high. The report on the urine examination is consistent with a failing liver, although we should expect to have seen many granular casts. The van den Bergh was naturally increased secondary to the intense jaundice. The bromsulfalein showed 95 per cent retention, a finding which is evidence of marked insufficiency such as that in acute yellow atrophy, if one can eliminate two other conditions, namely malignancy of the liver, in which case we should expect the liver to be large, and obstructive jaundice, which does not fit the history or various other findings, including the brown stools. The serum protein was 7.6 gm. per 100 cc., which is normal. This is surprising because we expect the protein to be low in cirrhosis, but if they had done the albumin-globulin ratio, I am sure that they would have found the albumin low and the globulin high, as suggested by the formol-gel test on the first admission.

A feature which is a little difficult to fit in is the story of typical gall-bladder colic (nausea, vomiting and severe pain requiring morphine). However, this is not entirely inconsistent because cirrhosis of the liver may give severe pain in the right upper quadrant. Therefore, though we cannot eliminate the diagnosis of gallstones, I do not believe we need to assume it on the basis of the information at hand. The story of clay-colored stools following the attack is suggestive of common-duct obstruction, but at least after the patient reached the hospital we find that the stools were normal in color.

I cannot explain the very low blood cholesterol unless the figure is a misprint.

Dr. James T. Heyl: It was re-checked in the laboratory and again found to be 49, the lowest value on record.

Dr. Urmy: I shall have to ask someone else to explain it.

It appears, then, that there was a portal cirrhosis

of the liver with acute failure in the last few weeks, no doubt in part precipitated by the administration of arsphenamine and the ingestion of alcohol. There is a possibility that a gallstone attack may have taken place, but I doubt it.

Two or three other things in the record should be discussed. The story of a fall with unconsciousness lasting three hours suggests a severe brain injury. There was no lucid period with subsequent loss of consciousness to suggest hemorrhage from the middle meningeal artery. There were severe headaches and nosebleeds coming on after a gap of one month. This combination usually raises the question of hypertension, but I doubt that a blood pressure of 150 systolic, 80 diastolic, could be called hypertension. In view of the head injury a month before, I think it is reasonable to assume the headaches were due to it. To be sure, dull headaches are not infrequent even early in the course of cirrhosis, but these headaches seem to have been more severe than one would expect in cirrhosis alone. The nosebleeds could have been a part of the generally increased tendency to bleed in cases of cirrhosis. I think we must assume there was some damage to the brain at the time of the fall and that it caused the headaches. The fact that the skull plate after admission did not show any abnormality, of course, does not rule out injury. The hospital neurological examination was not significant of anything more than mild paralysis agitans.

Dr. Tracy B. Mallory: Do you want to bring syphilis up at all?

Dr. Urmy: I should have brought that up in connection with the headaches. Central-nervous-system syphilis would have to be eliminated, and she should have had a lumbar puncture for that reason as well as for investigation of the headaches per se. Syphilis could, of course, have played a definite part in the etiology of her cirrhosis. I cannot explain the reason for the follicle-stimulating hormone test.

Dr. Mallory: Perhaps Dr. Heyl will tell us why it was done.

Dr. Heyl: Dr. Fuller Albright was interested in whether there was a Cushing's syndrome. She was studied completely from that point of view.

Dr. Holmes: In the x-ray films there are two or three things that in a negative way are of interest. I am always interested to see of how much value x-ray study is in determining the size of the liver. On physical examination the liver was said to be large; this was denied by the roentgenologist. In this film you can see the edge of the liver very distinctly here, and it is about opposite the twelfth rib posteriorly; so it seems as if it could not have been very large. The films of the skull are negative, but I should agree with Dr. Urmy that that does not mean anything. One other interesting thing is that diverticula sometimes show up much better after the colon is emptied than they do when it is full.

Dr. William B. Breed: Dr. Urmy, would you not be willing to reject Dr. Mallory's sly suggestion of syphilis? You seemed rather inclined to accept it partially. The only pertinent information we have is a positive Hinton test, a negative Wassermann test, many living children and several miscarriages. The fact must be remembered that syphilitic cirrhosis is a very unusual occurrence. I think it would be interesting for us to give Dr. Mallory a definite answer to the question, or at least an opinion. I should be willing to say that syphilis had not played a part in this woman's disease. Can we find what the impression about her was in the wards?

Dr. Heyl: As I remember it we had the impression that she was suffering from acute liver insufficiency, the three possible causative factors being arsphenamine, alcohol and syphilis, and that she died a death of severe liver insufficiency. We thought her liver must be small.

Clinical Diagnosis

Subacute yellow atrophy of the liver, with liver insufficiency.

Dr. Urmy's Diagnoses

Portal cirrhosis of the liver, with acute failure.
Head injury — type unknown.

Anatomical Diagnoses

Cirrhosis of the liver, old, type undetermined.
Subacute atrophy of the liver.
Jaundice.
Ascites.
Diverticula of the colon.
Hirsutism.

Pathological Discussion

Dr. Mallory: I wish I could answer some of the questions brought up by this case more definitely than I can. She certainly did not have a very large liver at the time of autopsy. It weighed just under 1500 gm., which is within the normal range for a woman. It showed, however, a very wrinkled, lax surface, and it cut with considerably increased resistance. On microscopic examination there was an obliteration of the normal architecture, a great deal of fibrosis which looked quite old and, finally, extensive, in fact almost complete, fresh necrosis of the remaining liver cells.

My guess would be that we were dealing with a fairly acute atrophy of a liver that was previously cirrhotic. That is perhaps too long a guess considering the limited amount of evidence that we have. If we assume that we are correct in supposing pre-existing cirrhosis, I am sure I do not know what it was other than portal. There was nothing to suggest that syphilis played any part in the picture. I think we should all like to know whether 3 oz. of whisky a day for six years was significant. I cannot answer that question. I think we have to attribute the terminal attack to the arsphenamine or the bismuth or both. The jaundice that is so commonly seen under those conditions must be attributed to liver damage, and I for one am sure that it may on occasion lead to atrophy. It is not unreasonable to suppose that the hazard is greater in a person with an already damaged liver, although the whole event can happen, I believe, with livers normal at the time the arsphenamine is started. She had no gall-bladder disease, no stones. The skull and brain were entirely negative. There was no evidence of a significant traumatic lesion. The pituitary and adrenal glands were both negative, thus ruling out any question of basophilism.

DR. HOLMES: Was the spleen enlarged?

DR. MALLORY: It was normal in size, weighing 125 gm.

DR. HOLMES: There was no evidence of varices?

DR. MALLORY: The man who did the examination thought he saw some minute varices. It is very difficult to be sure of small varices at autopsy. In the face of a normal-sized spleen I think the observation is doubtful.

DR. BREED: How toxic is bismuth to the liver?

DR. MALLORY: The rather common observation seems to be that the patients who are treated with arsphenamine sometimes develop jaundice immediately, but perhaps a little more frequently later, at a time when they are very apt to be getting bismuth. I believe the consensus is that with bismuth alone jaundice is very unusual. Can you answer that, Dr. Short?

DR. CHARLES L. SHORT: I should agree with what you have said.

The New England
Journal of Medicine
Formerly the
Boston Medical and Surgical Journal
Established in 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Official Organ of
The Massachusetts Medical Society
The New Hampshire Medical Society
The Vermont State Medical Society

Editorial Board

Joseph Garland, M.D. — John P. Sutherland, M.D.
William B. Breed, M.D. — Stephen Rushmore, M.D.
George R. Minot, M.D. — Hans Zinsser, M.D.
Frank H. Lahey, M.D. — Henry R. Viets, M.D.
Shields Warren, M.D. — Robert M. Green, M.D.
George L. Tobey, Jr., M.D. — Charles C. Lund, M.D.
C. Guy Lane, M.D. — John F. Fulton, M.D.
William A. Rogers, M.D. — A. Warren Stearns, M.D.
Dwight O'Hara, M.D.

Associate Editors

Thomas H. Lanman, M.D. — Donald Munro, M.D.
Henry Jackson, Jr., M.D.

Walter P. Bowers, M.D., Editor Emeritus
Robert N. Nye, M.D., Managing Editor
Clara D. Davies, Assistant Editor

Subscription Terms: $6.00 per year in advance, postage paid, for the United States; Canada, $7.04 per year; $8.52 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Saturday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

MEDICINE AND THE PRESENT CRISIS

For several years the Four Horsemen of the Apocalypse, mounted upon the steeds of Conquest or Plague, War, Famine and Death, have ravaged Asia and parts of Europe. Fear of the spread of their influence to the total involvement of civilization as we know it has been the concern of thoughtful men and women throughout the world, and the course of history during the past year has shown such fear to be well founded.

A crisis, then, exists, whether or not we choose to admit to ourselves its influence, immediate or remote, on our lives. Unpredictable and well-nigh incredible events have recently followed one another in rapid succession. Freedom of thought, speech and action in many parts of the world is on the defensive against the assaults of both political and ideological tyranny.

Medicine is no less influenced by the trends of world affairs than any other human activity. Although the ideals which it professes and the scientific foundations on which it is based are limited by no international boundaries, it is nevertheless true that both of these attributes may, under certain conditions, take divergent courses and pursue different purposes on the two sides of a hostile frontier. Although today, by the grace of God, medicine in the United States is not behind a hostile frontier, it should, like the nation of which it is a part, carefully survey and deliberate on its course in an uncertain future.

For the present two duties are apparent. The first lies within the realm of enlightened and patriotic self-interest, the second within the scope of professional relations. Both require study and application.

The vitality of a democratic society or nation, on which its survival is based, is derived from individual intelligence, realism and courage. The possession of one of these qualities without the other two, or of two without the third, does not suffice. That society or nation which is endowed with the highest intelligence will select the wisest course, provided it use realism to reject the appeals of prejudice, emotion and biased information (commonly known as propaganda) with which its intelligence is always assailed in times of crisis; the course thus selected, if adhered to with courage, will yield the most certain prospect of survival in an uncertain world. Medicine in the United States, although numerically but a small part of the nation which it serves, ranks high in the level of its intelligence. It should, however, study both world and national affairs, and by refusing to be led astray by prejudice, emotion and biased information attain the highest possible degree of realism. It should, both individually and collectively, place its reasoned opinions before the government which it has helped to create. Though there may be some who do not believe in the motto, *Vox populi, vox dei,* it is nevertheless true that the more audibly, intelligently and realistical-

ly the voice of the people is kept before the government which it has created to conduct its affairs and to guard its interests, the more nearly is achieved the ideal of a government of laws and not of men. Therefore alert, intelligent, realistic and courageous citizenship becomes the first duty at all times of the American physician and American medicine.

In the realm of professional relations the duty of medicine is no less clear. The healing art is designed to restore to health not only the diseased body and the deranged mind, but also to guide the emotions under control of the intellect. If medicine, by its moral and civic example, and by its therapeutic precepts, can instill into those to whom it renders service not only physical health but also emotional balance and clarity of perception and reasoning it will have done its duty amply in preparing our country for any adjustments or hardships which the future may bring.

RED CROSS MEMBERSHIP

Red Cross membership serves a double-barreled purpose. From the rosters of those who annually join the organization during Roll Call are drawn the volunteer workers who conduct most of the organization's work. From membership dues it derives the funds needed to carry on its day-to-day activities. Only in times of great disaster are special contributions and gifts requested.

During the past year Red Cross volunteers produced 720,000 pages of Braille reading matter for the blind. In some cases these pages were printed from aluminum or other plates, necessitating presses, in others each page was made up individually. Special paper had to be used. Each page had to be coated with a special shellac. Volumes had to be bound. Each operation cost a small amount. When costs are multiplied by 720,000 the result is a sizable figure.

Other Red Cross volunteers during the year produced 330,000 garments for disaster victims and others in need. In many cases the cloth had to be bought. The garments had to be sewed, necessitating sewing machines, needles and thread. The net cost of each garment was not great, but 330,000 such garments represent a considerable expenditure.

During the past year full-time professional public-health nurses employed by the national organization and its chapters made more than 1,000,000 visits to or on behalf of the sick and examined thousands of school and pre-school children. The cost of each visit and each examination was comparatively negligible, but by the time that figure is multiplied by more than one million, the sum runs into six figures.

Likewise 313,000 persons received instruction in first aid to the injured, another 100,000 were trained in water-rescue methods, and 2720 highway emergency first-aid stations and 2424 mobile first-aid units were being maintained as of July 1. During the year 40,000 men in the active armed forces of the United States, 165,000 veterans and 116,000 civilians, or families and dependents of these three classifications, were provided assistance in presenting government claims, in readjusting themselves to new conditions and in meeting various forms of distress. Again, each person trained in first-aid and water-rescue work, each first-aid station or unit, or each individual or family assisted, represents a comparatively small outlay; but when these numbers run well into the hundreds of thousands, it requires no imagination to see that their ultimate total annual cost mounts into money.

There are many other avenues along which the Red Cross combats human suffering. Anyone will realize there is no particular limit to its activities. Allowance must be made, not only for their continuance, but for their expansion. This growth of Red Cross services can only come with an increased membership — more members to volunteer their services in unselfish devotion to humanity, more members whose annual dues, though individually small, will finance continued growth of the Red Cross.

Besides the need of providing for Red Cross expansion, the present world uncertainty may bring great humanitarian problems. Though charity begins at home and the primary obligation of the Red Cross is to American citizens, Norman H.

Davis, the organization's chairman, has said: "The American Red Cross must, within the limit of its resources, extend aid to the victims of disaster in the world neighborhood in which we live. Charity is not worthy of its name if it ends at home."

It is for these reasons the Red Cross this year has set itself to enroll 1,000,000 additional members. Out of a population of 130,000,000 it is seeking some 6,600,000 who believe in extending a helping hand to those less fortunate than themselves. The annual Roll Call, when chapters the country over issue an invitation to join their ranks and thus enable the Red Cross not only to keep abreast of demands, but to prepare for any emergency, began November 11 and ends November 30.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

SEPTIC ABORTION

Mrs. M., a twenty-seven-year-old para II, entered the hospital on the morning of July 31, 1939, when about ten weeks pregnant. She had begun to flow a little on June 28 and had been flowing bright blood every day since July 1 sufficient to require at times the wearing of a heavy bath towel.

The family history was noncontributory. The patient had had mumps, measles and chickenpox. In 1937 she had had scarlet fever. An appendectomy had been performed in 1930. Catamenia began at twelve, were regular with a twenty-eight-day cycle and lasted four days. Her last period had begun on May 14. Her previous pregnancy, six years before, had been normal in every respect.

Examination on entrance showed a well-developed, very pale woman. The heart was not enlarged; there were no murmurs. The lungs were clear and resonant; there were no rales. The abdomen was soft, with a right-rectus appendectomy scar. Vaginal examination showed the fundus to be retroverted and enlarged. There was some fresh bleeding. The temperature on admission was 100°F., the pulse 80.

The afternoon temperature on the day of entry was 102°F., the pulse 100. She had a chill that night with a temperature rise to 106°F. and a pulse rise to 140. The next morning the temperature was 100°F., but in the afternoon rose to 104 with a pulse of 120. She continued to bleed freely, and on August 2 she was transfused with 500 cc. of citrated blood. She was seen in consultation, and a diagnosis of septic abortion was made. Because of the continued bleeding, exploration of the uterus was advised. Although the temperature following another chill had risen to 105°F., this procedure was carried out on August 4. At the time of operation she was given a second transfusion, consisting of 500 cc. of citrated blood. The uterus was explored digitally and a considerable amount of adherent placental tissue was removed; the bleeding promptly ceased. The temperature came down to normal the following day and remained normal.

The red-blood-cell count on August 1 was 3,400,000, and the hemoglobin 70 per cent. On August 4 before operation the red-cell count was 2,200,000, the hemoglobin 48 per cent. Blood cultures showed no growth. Vaginal cultures on two occasions showed a few colonies of *Staphylococcus aureus* and moderate number of *Bacillus coli*. The cultures from the uterus at the time of operation showed *Staphylococcus aureus*.

She remained in the hospital for five days after the operation and was discharged relieved at the end of that time.

Comment. This case represents the ideal treatment for a septic abortion complicated by hemorrhage. Although the temperature was ranging from 100 to 105°F., the uterus was left alone until continued hemorrhage made its invasion necessary. The patient had bled so much before entering the hospital that a transfusion was done two days later. In spite of this transfusion her red-cell count on the morning of operation had fallen to 2,200,000 from 3,400,000. The routine of starting transfusion at the time of the operation is worthy of note. During the operation considerable blood was lost, which was immediately made up for by the transfusion. The invasion of the uterus was carried out because of hemorrhage and done in the gentlest manner possible. The handling of the case from the beginning to the end was ideal.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions of the Medical Postgraduate Extension Courses have been arranged for the week beginning November 20:

BARNSTABLE

Sunday, November 26, at 4:00 p.m., at the Cape Cod Hospital, Hyannis. Syphilis in Pregnancy and

the Offspring. Instructor: William P. Boardman. Donald E. Higgins, *Chairman.*

BRISTOL NORTH

Thursday, November 23, at 4:00 p.m., at the Morton Hospital, Taunton. Pneumonia. Instructor: W. Barry Wood, Jr. Lester E. Butler, *Chairman.*

BRISTOL SOUTH (New Bedford Section)

Friday, November 24, at 4:00 p.m., at St. Luke's Hospital, New Bedford. Cardiovascular Disease: Eleven important questions about heart disease and their answers. Instructor: Bernard J. Walsh. Robert H. Goodwin, *Chairman.*

ESSEX NORTH

Friday, November 24, at 4:30 p.m., at the Lawrence General Hospital, Lawrence. Common Problems of Neurology: Indications for lumbar puncture. Instructor: T. J. C. von Storch. John Parr, *Chairman.*

ESSEX SOUTH

Tuesday, November 21, at 4:00 p.m., in the Conference Room of the Salem Hospital, Salem. Convulsions in Infants and Children — Etiology and Treatment. Instructor: John A. V. Davies. J. Robert Shaughnessy, *Chairman.*

MIDDLESEX EAST

Tuesday, November 21, at 4:00 p.m., at the Melrose Hospital, Melrose. Gonorrhea in the Female. Instructor: Alonzo K. Paine. Walter H. Flanders, *Chairman.*

MIDDLESEX NORTH

Friday, November 24, at 4:45 p.m., at St. John's Hospital, Lowell. Head and Spine Injuries. Instructor: Walter R. Wegner. William S. Lawler, *Chairman.*

WORCESTER (Milford Section)

Tuesday, November 21, at 8:30 p.m., in the Nurses' Home of the Milford Hospital, Milford. Common Problems of Neurology: Indications for lumbar puncture. Instructor: H. Houston Merritt. Joseph Ashkins, *Chairman.*

WORCESTER (Worcester Section)

Friday, November 24, at 8:00 p.m., in the Staff Room of the Worcester City Hospital, Worcester. War Gases. Instructor, G. Philip Grabfield. George C. Tully, *Chairman.*

WORCESTER NORTH

Friday, November 24, at 4:30 p.m., in the Nurses' Home of the Burbank Hospital, Fitchburg. Convulsions in Infants and Children — Etiology and Treatment. Instructor: Louis K. Diamond. George P. Keaveny, *Chairman.*

DEATHS

HALLETT — EDWARD B. HALLETT, M.D., of Gloucester, died November 8. He was in his seventy-sixth year.

Born in Yarmouthport, he received his degree from Dartmouth Medical School in 1887 and served his internship at the Chelsea Marine Hospital. He settled in Gloucester fifty-one years ago and until five years ago was port doctor for the United States Public Health Service. Dr. Hallett was a former president of the medical staff of the Addison Gilbert Hospital in Gloucester.

He was a member of the Massachusetts Medical Society and a fellow of the American Medical Association.

His widow, a son, Dr. Ronald P. Hallett, a daughter and a sister survive him.

PAGE — PEIRSON S. PAGE, M.D., of Andover, died May 23. He was in his sixty-eighth year.

Born in Williamsport, Pennsylvania, he attended the University of the State of New York and the International Y. M. C. A. Training School in Springfield, Massachusetts. In 1899 he received his degree from University and Bellevue Hospital Medical College.

Dr. Page was master of physical education at Phillips Academy, Andover, having held this position since 1902. He helped to build the school infirmary in 1912 and before he died a new addition to it was completed, largely under his direction.

He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow and four daughters survive him.

MISCELLANY

DIRECTORY OF MEDICAL SPECIALISTS

The Advisory Board for Medical Specialties will issue in December the first edition of the *Directory of Medical Specialists,* listing approximately 14,000 specialists certified by the twelve American boards and the two affiliate boards.

This directory will have three sections. The first will be devoted to a brief discussion of the Advisory Board for Medical Specialties, its organization and objectives. The second section will have fourteen separate divisions, one for each American board, with a geographic and a detailed biographic listing of its diplomates. Each of these divisions will give full information regarding requirements for admission to examinations for certification, details of organization of each board, and other general information. The third and final section will be a complete alphabetic list of all 14,000 diplomates, with their addresses and indications of specialty certification.

It is expected to issue the directory every two years. No charge is made for listing in the directory, and only the names of the specialists certified by the American boards will be included. The directory represents an effort officially to inform the lay and medical public regarding the present strong movement for certification of qualified medical specialists.

Financial support has been given the directory by the American boards; the project is not designed to be profit-making, and the widest possible public distribution of the directory is desired. On these accounts, the subscription price of the book has been set at a sum ($3.50 per copy) computed to cover only publication expenses.

The directory should be invaluable to the entire medical profession in the reference of patients, as well as in many other ways, and the individual support of this new project of the American boards is earnestly solicited of every diplomate. The directory will be sold generally to physicians, libraries, hospitals and others by subscription. Such subscriptions may be made through the Columbia University Press, 2960 Broadway, New York City, or through the office of the directing editor, Dr. Paul Titus, 1015 Highland Building, Pittsburgh, Pennsylvania.

NOTE

Dr. Charles T. Porter, of Boston, was elected third vice-president of the American Academy of Ophthalmology and Otolaryngology at the recent annual meeting in Chicago. Among the appropriations for research was one of four hundred dollars to Dr. Moses H. Lurie, instructor in otology, Harvard Medical School, for studies on the balancing apparatus of the ear.

CORRESPONDENCE

CANCER AS A PUBLIC-HEALTH PROBLEM

To the Editor: In the editorial on "The National Cancer Institute" in a recent issue of the *Journal* you gave credit properly to the late Drs. G. H. Bigelow and R. B. Greenough for splendid work in the early days following the recognition of cancer as a public-health problem in the State of Massachusetts. You neglected, however, to refer to the pioneer work of Dr. Francis D. Donoghue, who was largely responsible for legislative action establishing the Pondville Hospital under the Massachusetts Department of Public Health over the protests of many public-health authorities. I am sure that the failure to refer to Dr. Donoghue's part in this work was an oversight which should be corrected.

TIMOTHY LEARY, M.D.

784 Massachusetts Avenue,
Boston, Mass.

TELEPHONE RATES FOR PHYSICIANS

To the Editor: I enclose a copy of a letter from Mr. Ash of the New England Telephone and Telegraph Company, which I believe will be of interest to the readers of the *Journal*.

ELMER S. BAGNALL, M.D.

281 Main Street,
Groveland, Massachusetts.

* * *

Dear Dr. Bagnall:

I am very glad to outline, as you recently requested, the regulations regarding the application of business or residence telephone rates for physicians.

Business rates usually apply for telephone service installed in the office of a physician, surgeon, dentist, veterinary surgeon, chiropractor, osteopath or other medical practitioner or of a clergyman or Christian Science practitioner or other persons actively engaged in a professional pursuit, when the office is used for the business purposes of the individual or of the organization with which he is connected, whether the office is located in the residence or in another building. When a practicing physician is not a subscriber to or joint user of business service, or a habitual user of it at another location, as at a hospital, there is a presumption of substantial business use of the service in his name at his residence, although such circumstances cannot be considered conclusive.

When a listing is requested containing a word or an abbreviation clearly indicative of the subscriber's profession (physician, dentist and so forth) it should be considered that the applicant has definitely stated that the use of the associated service at his residence is primarily for occupational purposes and business rates apply. However, a simple abbreviated title such as is ordinarily used in addressing the individual concerned, for example, "Dr." or "Rev.," is not considered as clearly indicative of a substantial occupational use of the service, and if the use of the service at the residence is primarily for social or domestic purposes, residence rates apply. When the listing contains such a title and the subscriber admits that the use of his service is primarily for occupational purposes or when he does not concede this fact but the evidence clearly indicates that this is the primary use of the service, business rates apply.

DANA H. ASH, *Manager,*
New England Telephone
and Telegraph Company.

Haverhill, Massachusetts.

ARTICLES ACCEPTED BY THE AMERICAN MEDICAL ASSOCIATION COUNCIL ON PHARMACY AND CHEMISTRY

To the Editor: In addition to the articles enumerated in our letter of September 15 the following have been accepted:

Abbott Laboratories
- Alternaria spp., Fungus Extract 5 per cent — Abbott
- *Aspergillus fumigatus,* Fungus Extract 5 per cent — Abbott
- *Aspergillus niger* Group, Fungus Extract 5 per cent — Abbott
- *Cephalothecium roseum,* Fungus Extract 5 per cent — Abbott
- Hormodendrum spp., Fungus Extract 5 per cent — Abbott
- *Monilia sitophilia,* Fungus Extract 5 per cent — Abbott
- Mucor spp., Fungus Extract 5 per cent — Abbott
- *Penicillium rubrum,* Fungus Extract 5 per cent — Abbott
- *Ustillago zeae* (corn smut), Fungus Extract 5 per cent — Abbott
- Yeast, Fungus Extract 5 per cent — Abbott
- Tablets Barbital — Abbott, 5 gr.

Armour Laboratories
- Gastric Mucin — Armour
- Gastric Mucin Powder — Armour
- Gastric Mucin Granules — Armour

Baxter Laboratories
- Sodium Citrate 2½ per cent in Physiological Sodium Chloride Solution in the Transfuso Vac and Donor Set

Gilliland Laboratories
- Typhoid-Paratyphoid Bacterial Vaccine, Immunizing, 50 cc. vial

International Vitamin Corp.
- I. V. C. Cod Liver Oil

Lederle Laboratories, Inc.
- Capsules Sulfapyridine — Lederle, 0.25 gm.

National Drug Co.
- Immune Globulin (Human) 2 cc. ampule-vial
- Immune Globulin (Human) 10 cc. ampule-vial

Smith – Dorsey Co., Inc.
- Tablets Sulfanilamide, 5 gr.

E. R. Squibb & Sons
- Ascorbic Acid — Squibb
- Tablets Ascorbic Acid — Squibb, 25 mg.

Tablets Ascorbic Acid — Squibb, 50 mg.

Frederick Stearns & Co.
Gastric Mucin — Stearns
Gastric Mucin Powders — Stearns
Gastric Mucin Granules — Stearns

Wallace & Tiernan Products, Inc.
Azochloramid Saline Mixture 1:3300 Tablets, 8.5 gr.

The Wilson Laboratories
Gastric Mucin — Wilson
Gastric Mucin Powder — Wilson
Gastric Mucin Granules — Wilson

Winthrop Chemical Co., Inc.
Fuadin
Ampules Solution Fuadin, 3.5 cc.
Ampules Solution Fuadin, 5 cc.

PAUL NICHOLAS LEECH, *Secretary.*

535 North Dearborn Street,
Chicago, Illinois.

REPORT OF MEETING

FOUR COUNTY MEDICAL SOCIETY

The annual meeting of the Four County Medical Society, comprising the Berkshire, Franklin, Hampden and Hampshire district medical societies, was held at Springfield, on Tuesday, October 10. The subject under discussion was: "Pain: Its significance in diagnosis and prognosis." This was discussed from the viewpoint of general medicine by Dr. Lewis M. Hurxthal, Boston, from that of general surgery by Dr. Arthur W. Allen, Boston, from that of gynecology by Dr. Joe V. Meigs, Boston, and from that of neurology by Dr. Foster Kennedy, professor of clinical neurology, Cornell University Medical School, New York City.

Following the meeting, a luncheon in honor of Dr. Walter G. Phippen, president of the Massachusetts Medical Society, was held at the Hotel Stonehaven, with approximately 100 members attending. During the luncheon the following list of officers was submitted and elected for the ensuing year: president, Dr. George L. Schadt, Springfield; secretary, Dr. W. Fenn Hoyt, Springfield; vice-presidents, Dr. Hugh J. Downey, Pittsfield, Dr. Frederick J. Barnard, Greenfield, Dr. John M. Murphy, Florence, and Dr. Frederic Hagler, Springfield. It was voted to hold the next annual meeting at Greenfield.

NOTICES

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, November 22, from 2 to 4 p.m. Drs. Elliott C. Cutler and Soma Weiss will speak on "Headache." A clinicopathological conference, conducted by Dr. Elliott C. Cutler, will take place from 4 to 5 p.m.

On Thursday, November 23, from 8:30 to 9:30 a.m. there will be at the Children's Hospital, a combined clinic, conducted by Dr. Kenneth D. Blackfan, of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital.

Physicians and students are cordially invited to attend.

ELLIOTT C. CUTLER, M.D., *Secretary.*

BOSTON CITY HOSPITAL

The next clinical meeting of the Boston City Hospital will be held in the Cheever Amphitheater, Thursday, November 23, at 11:30 a.m. The subject "Water Metabolism" will be discussed in the manner of "Information Please."

Meetings are planned to be held in the Cheever Amphitheater the last Thursday of every month from November to May, excepting December.

H. K. THOMPSON, M.D., *Chairman,*
Committee on Hospital Clinics.

BOSTON MEDICAL HISTORY CLUB

There will be a meeting of the Boston Medical History Club at the Boston Medical Library, 8 Fenway, Boston, on Monday evening, November 20, at 8:15. Professor Richard H. Shryock, professor of American history, University of Pennsylvania, will talk on "The Historian Looks at Medicine."

All those interested in the subject are cordially invited to attend.

PAUL D. WHITE, M.D., *President,*
BENJAMIN SPECTOR, M.D., *Secretary.*

BOSTON LYING-IN HOSPITAL

Dr. A. Louis Dippel will speak on "Visualization of Placenta in Utero" at the Boston Lying-in Hospital, on Tuesday evening, November 28, at 8:15.

Members of the medical profession are cordially invited to attend.

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra will rehearse under Alexander Theide, former concertmaster with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra, every Thursday at 8:30 p.m., in Studio A, Station WMEX, 70 Brookline Avenue, Boston. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

BETH ISRAEL HOSPITAL

Professor Bernhard Zondek will lecture on "Inhibition of the Anterior Pituitary Function Through the Estrogenic Hormone" with illustrated lantern slides at the auditorium of the Beth Israel Hospital on Saturday morning, November 18, at 10:30.

Physicians and medical students are cordially invited to attend.

UNIVERSITY EXTENSION COURSES

A university extension course on "Practical X-Ray" designed for technicians, nurses, medical secretaries and others who need to know more about the subject is to be given by the Massachusetts Department of Education on Thursday evenings, at 7:45 o'clock, in Harvard Hall, Harvard University. The first meeting of the class will be on November 23.

The class will be led by Max Ritvo, M.D., instructor in

roentgenology, Harvard Medical School. The lectures will cover the history and theory of x-rays and the design and operation of different x-ray machines and tubes. Applications to medicine, science, industry and the arts will be discussed and illustrated extensively by films and lantern slides. X-ray and radium treatment of diseases also will be touched on briefly.

MASSACHUSETTS HOSPITAL ASSOCIATION

The third mid-year dinner meeting of the Massachusetts Hospital Association will be held at the Parker House, Boston, on Tuesday, December 5, at 6:30 p.m.

MASSACHUSETTS SOCIETY OF EXAMINING PHYSICIANS

There will be a meeting and dinner of the Massachusetts Society of Examining Physicians at the Copley-Plaza Hotel on Wednesday evening, November 22, at 6:30. Dinner will be $2.50 per plate.

PROGRAM

Narcotics. Assistant United States Attorney William T. McCarthy, in charge of the Criminal Division.

The Cause and Manner of the Squalus Deaths. Dr. William J. Brickley.

MATTHEW V. NORTON, M.D., *President,*
WILLIAM P. COUES, M.D., *Secretary.*

WACHUSETT MEDICAL IMPROVEMENT SOCIETY

A meeting of the society will be held at Holden District Hospital on Wednesday, December 6, at 6:30 p.m. Dr. John Dumphy, of Worcester, will speak on "Sulfanilamide, Sulfapyridine and Related Compounds."

Members of the profession are cordially invited to attend.

LEROY E. MAYO, M.D., *Secretary.*

NEW ENGLAND HEART ASSOCIATION

The next meeting of the New England Heart Association will be held at the Massachusetts General Hospital, on Monday, November 27, at 8:15 p.m.

PROGRAM

Demonstration of Specimens. Dr. Paul D. White.

Non-luetic aortic aneurysms: dissecting aneurysm of the aorta followed a year and a half later by a new dissecting aneurysm of the aorta with rupture and death.

Arteriosclerotic thoracic aortic aneurysm with rupture.

Healed subacute bacterial endocarditis in a heart showing active rheumatic myocardial involvement.

Variations in PR Interval and Duration of the QRS Waves in the Classic Leads: The possibility of error in the measurements. Drs. P. D. White, C. E. Leach and S. A. Foote.

Demonstration of Lag Screen for Visualization of Electrocardiogram (Cardioscope). Dr. H. B. Sprague.

The Clinical Significance of Low Voltage of the QRS Waves in the Classic Leads and Lead 4. Drs. C. E. Leach and P. D. White.

An Autopsy Study of the Relations of Gall-Bladder Disease and of Peptic Ulcer to Coronary Disease. Drs. B. J. Walsh, E. F. Bland and P. D. White.

A Note on Vagotonia and Coronary Disease. Dr. Alberto Taquini.

Subacute Bacterial Endocarditis. Drs. S. Kelson and P. D. White.

Analysis of 250 cases from 1924 to 1938 inclusive; with particular reference to diagnosis and prognosis.

New therapy: sulfapyridine and heparin combined.

Cervicothoracic Sympathectomy in Preference to Paravertebral Alcohol Injection for Angina Pectoris with High Radiation of Pain: New technic. Drs. J. C. White and H. B. Sprague.

Interested physicians and medical students are cordially invited to attend.

EDWARD F. BLAND, M.D., *Secretary.*

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The written examination and review of case histories (Part I) for Group B candidates will be held in the various cities of the United States and Canada on Saturday, January 6, 1940, at 2:00 p.m. Formal notice of the place of examination will be sent each candidate several weeks in advance of the examination date. No candidate will be admitted to examination whose examination fee has not been paid at the secretary's office. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination held in June, 1940. Receipt of Group B applications for the current examination (January 6, 1940) closed October 4.

Candidates who are required to take re-examinations must do so before the expiration of three years from the date of their original examination.

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted by the entire board, meeting in Atlantic City, New Jersey, on June 8, 9, 10 and 11, 1940, immediately prior to the annual meeting of the American Medical Association in New York City.

Application for admission to Group A, Part II, examinations must be on file in the secretary's office not later than March 15, 1940.

After January 1, 1942, there will be only one classification of candidates, and all will be required to take the Part I and Part II examinations. For further information and application blanks, address Dr. Paul Titus, secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, NOVEMBER 20

MONDAY, NOVEMBER 20

*11:30 a.m. Carney Hospital. Monthly clinical meeting and luncheon.

*12:15 p.m.–1:15 p.m. Clinicopathological conference. Dr. S. Burt Wolbach, Peter Bent Brigham Hospital amphitheater.

*8:15 p.m. Boston Medical History Club. Boston Medical Library, 8 Fenway, Boston.

TUESDAY, NOVEMBER 21

*9-10 a.m. "Personality of the Criminal." Dr. A. Warren Stearns. Joseph H. Pratt Diagnostic Hospital.

*10 a.m.–12:30 p.m. Boston Dispensary tumor clinic.

*12 m. South End Medical Club. Headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston.

*12:15 p.m.–1:15 p.m. X-ray conference. Dr. Merrill C. Sosman. Peter Bent Brigham Hospital amphitheater.

WEDNESDAY, NOVEMBER 22

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12 m. Clinicopathological conference. Children's Hospital amphitheater.

*2 p.m.–4 p.m. Joint medical and surgical clinic. Peter Bent Brigham Hospital.

6:30 p.m. Massachusetts Society of Examining Physicians. Copley-Plaza Hotel, Boston.

THURSDAY, NOVEMBER 23

*8:30 a.m.–9:30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Children's Hospital.

*9–10 a.m. Diabetic Clinic. Dr. Joseph Rosenthal. Joseph H. Pratt Diagnostic Hospital.

11:30 a.m. Boston City Hospital. Clinical meeting.

FRIDAY, NOVEMBER 24

*9–10 a.m. Clinicopathological conference. Dr. Soma Weiss and Dr. Rudolf Osgood. Joseph H. Pratt Diagnostic Hospital.

*10 a.m.–12:30 p.m. Boston Dispensary tumor clinic.

SATURDAY, NOVEMBER 25

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*10 a.m.–12 m. Medical staff rounds of the Peter Bent Brigham Hospital. Conducted by Dr. Soma Weiss.

*Open to the medical profession.

NOVEMBER 17 — Boston Lying-in Hospital. Page 758, issue of November 9.

NOVEMBER 18 — Beth Israel Hospital, Boston. Page 797.

NOVEMBER 20 — Carney Hospital. Monthly clinical meeting and luncheon. Page 759, issue of November 9.

NOVEMBER 20 — Boston Medical History Club. Page 797.

NOVEMBER 21 — South End Medical Club. Page 759, issue of November 9.

NOVEMBER 21 — Lawrence Cancer Clinic. Page 759, issue of November 9.

NOVEMBER 22 — Peter Bent Brigham Hospital. Joint medical and surgical clinic. Page 797.

NOVEMBER 22 — Massachusetts Society of Examining Physicians. Page 798.

NOVEMBER 23 — Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital. Page 797.

NOVEMBER 23 — Boston City Hospital. Clinical meeting. Page 797.

NOVEMBER 24 — Boston Dispensary. Luncheon meeting of the clinical staff. Page 758, issue of November 9.

NOVEMBER 25 — Joseph H. Pratt Diagnostic Hospital. Page 758, issue of November 9.

NOVEMBER 27 — New England Heart Association. Page 798.

NOVEMBER 28 — Boston Lying-in Hospital. Page 797.

DECEMBER 2 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

DECEMBER 5 — Massachusetts Hospital Association. Page 798.

DECEMBER 6 — Wachusett Medical Improvement Society. Page 798.

DECEMBER 6 — New England Obstetrical and Gynecological Society. Page 759, issue of November 9.

DECEMBER 8 — William Harvey Society. Page 676, issue of October 26.

DECEMBER 14 — Pentucket Association of Physicians. 8:30 p.m., Hotel Bartlett, Haverhill.

JANUARY 6, JUNE 8–11, 1940 — American Board of Obstetrics and Gynecology. Page 160, issue of July 27, and page 798.

JANUARY 22–25, 1940 — American Academy of Orthopaedic Surgeons. Hotel Statler, Boston.

FEBRUARY 11–14 — International College of Surgeons. Page 759, issue of November 9.

MARCH 2, JUNE 8 and 10 — American Board of Ophthalmology. Page 719, issue of November 2.

MARCH 7–9, 1940 — The New England Hospital Association. Hotel Statler, Boston.

MAY 14, 1940 — Pharmacopoeial Convention. Page 894, issue of May 25.

JUNE 7–9, 1940 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH

JANUARY 3, 1940 — Semi-annual meeting. Combined meeting with Essex South. Danvers State Hospital, Hathorne. 7 p.m.

ESSEX SOUTH

DECEMBER 6 — "Pyelonephritis and Its Relation to Other Inflammatory Diseases of the Kidney." Dr. Soma Weiss. Salem Hospital, Salem.

JANUARY 3, 1940 — "Head Injuries." Dr. John S. Hodgson. Danvers State Hospital, Hathorne.

FEBRUARY 14 — "Cough, Sputum, Hemoptysis — How shall they be investigated?" Dr. Reeve H. Betts. Essex Sanatorium, Middleton.

MARCH 6 — "Experimental and Clinical Considerations of Sulfanilamide Treatment of Hemolytic Streptococcal Infections." Dr. Champ Lyons. Lynn Hospital, Lynn.

APRIL 3 — Addison Gilbert Hospital, Gloucester.

MAY 8 — Annual meeting. Salem Country Club, Peabody.

HAMPSHIRE

JANUARY 10, 1940.

MARCH 13.

MAY 8.

All meetings are held at 11:30 a.m. at the Cooley Dickinson Hospital, Northampton.

MIDDLESEX EAST

JANUARY 10, 1940.

MARCH 20.

MAY 15.

Meetings are held at 12:15 p.m. at the Unicorn Country Club, Stoneham.

PLYMOUTH

JANUARY 18, 1940 — Brockton Hospital, Brockton.

MARCH 21 — Goddard Hospital, Brockton.

APRIL 18 — State Farm.

MAY 16 — Lakeville Sanatorium, Lakeville.

SUFFOLK

NOVEMBER 29 — Scientific meeting. Treatment of Syphilis. Dr. Harold T. Hyman, Dr. Louis Chargin, and Dr. William Leifer, of New York City.

JANUARY 31, 1940 — Scientific meeting. Subject to be announced later.

MARCH 27 — Scientific meeting. Symposium on Ulcerative Colitis and Diarrheas. Under the direction of Dr. Chester M. Jones.

APRIL 24 — Annual meeting in conjunction with the Boston Medical Library. Election of officers. Program and speakers to be announced later.

BOOKS RECEIVED FOR REVIEW

Nursing Mental Diseases. Harriet Bailey. Fourth edition. 264 pp. New York: The Macmillan Co., 1939. $2.50.

Infections of the Hand. Lionel R. Fifield. Second edition by Patrick Clarkson. 167 pp. New York: Paul B. Hoeber, Inc., 1939. $3.25.

A Textbook of Pathology for Nurses. Coleman B. Rabin. Second edition, revised. 260 pp. Philadelphia and London: W. B. Saunders Co., 1939. $1.75.

An Introduction to Genetics. A. H. Sturtevant and G. W. Beadle. 391 pp. Philadelphia and London: W. B. Saunders Co., 1939. $3.25.

Laboratory Manual for Animal Histology. Clair A. Hannum. Third edition. 105 pp. Tucson: University of Arizona, 1939. $1.75.

Injuries of the Nervous System: Including poisonings. Otto Marburg and Max Helfand. 213 pp. New York: Veritas Press, 1939. $3.00.

BOOK REVIEWS

Clinical Studies in Psychopathology: A contribution to the aetiology of neurotic illness. Henry V. Dicks. 248 pp. Baltimore: William Wood & Co., 1939. $4.75.

The material of this volume originally formed a series of postgraduate lectures given at the Tavistock Clinic as part of a larger course in psychotherapy. According to the author, the subject matter necessitated an acquaintance with the major modern schools of psychotherapy; therefore, it lays no claim to originality, and merely represents the contribution of one individual to current discussions of the psychoneuroses. It is based on the contributions of Freud and of those who, according to the author, have extended Freud's teachings (Jung and Adler).

The volume discusses, in turn, anxiety and obsessional states, hysteria, ambivalence, drug addictions, sexual perversions and inversions and abnormalities in sexual function. The author omits any detailed discussions of such important psychopathological states as reactive depressions, character disorders and organ neuroses, although in the last chapter he gives an outline of his general ideas on these subjects.

The theoretical part of the book is illustrated by sixty-two clinical histories, and by means of this material, he formulates three main instinctive tendencies — the self-preservative, the sexual (Freud's libido concept) and the aggressive. It appears to the reviewer that this formulation of the instincts is too artificial, as no instinctive drive ever appears in pure culture, but is admixed, frequently overlaps and is subject to complicated vicissitudes.

The author is an eclectic, although on every major point he is in agreement with the dynamic formulations of Freud. He emphasizes that in psychoanalytic therapy we have a weapon of attack on the neuroses which answers to the requirements of science. However, in order to shorten the psychotherapeutic procedures, he tends to direct the free associations by attempting to keep the associations to a stimulus idea, namely the most important symptom. This technical procedure somewhat resembles the obtaining of an associative anamnesis. In conclusion he states what psychoanalysis has emphasized almost from its beginnings: that analytic treatment is directed not only to a removal of symptoms, but also to an altering of the personality in the direction of social and psychologic maturity.

Public Health Law. James A. Tobey. Second edition. 414 pp. New York: The Commonwealth Fund, 1939. $3.50.

This second edition deals with much of historical and evolutionary interest in the development of our present-day public-health laws. The material contained is of primary importance to public-health administrators, and none should dabble in legislative matters pertaining to public health without some such guide to reliable and authoritative sources of legal information. Something over two thousand cases are referred to and indexed. Some general principles are enunciated; for example, laws should be enacted for enforcement only, never for educational purposes. It is of interest to note that Congress created a National Board of Health in 1879. It died because it was not, as we now say, "adequately implemented." Altogether the book is a very worthwhile compilation.

Les Occlusions Artérielles Aigues des Membres: Formes cliniques, indications physiopathologiques et therapeutiques. H. Haimovici. 124 pp. Paris: Masson et Cie, 1939. 26 Fr. fr.

This is a stimulating little book on all phases of acute occlusions of the peripheral arteries including both thrombosis and embolism and touching on other causes that are uncommon. Because the material is almost entirely clinical, the practitioner will find this book handy for quick reference.

The author emphasizes the role of vasomotor spasm in acute occlusions and suggests the relief of this spasm by medication or sympathetic attack before the performance of embolectomy. Obviously influenced by Lériche, he moreover advises the excision of the thrombosed artery, regardless of whether the process be primary, or secondary to an embolus. He attempts no evaluation of suction-pressure therapy in these conditions.

The author comes from a group of men who have promoted our knowledge of the interrelation of diseases of the arteries and the veins, and one therefore finds a pertinent discussion of the venous complications of acute arterial involvement.

The absence of plates and the lack of a good bibliography are somewhat disappointing.

The Hair and Scalp: A clinical study. Agnes Savill. Second edition. 309 pp. Baltimore: William Wood & Co., 1937. $4.75.

This book is an amplification and revision of the first edition, but the general arrangement remains the same, in that diseases are considered according to symptom or sign rather than etiology. The latter makes easy the identification of the particular scalp trouble at hand by those untrained in dermatology.

After a chapter on the structure and physiology of the hair, gray hair is taken up, with advice not to dye it, although in a later chapter the subject of dyeing is extensively discussed and its disadvantages pointed out. The author advises extensive brushing and combing of the hair, disposes of the superstition that cutting a woman's hair short stimulates its growth, and shows by microscopic study that singeing is somewhat harmful. She very sensibly advises washing the hair when it needs it rather than by any set schedule of weeks; she shows that some, at least at times, may need to wash the hair every day and without any harm whatever so long as it is carefully done and properly dried, whereas other scalps remain so clean in regions of clear atmosphere that they may not need washing for months.

The book is written for the general practitioner, who will find many helpful points. Although the dermatologist might prefer a more scientific arrangement, he will find the book very useful.

Epidemic Encephalitis: Etiology, epidemiology, treatment. Third report by the Matheson Commission. 493 pp. New York: Columbia University Press, 1939. $3.00.

The Matheson Commission for the Study of Epidemic Encephalitis, established in 1927, has published two previous reports on the subject (1929 and 1932). Both of these proved invaluable to investigators, as well as to public-health officials. In the last seven years, much new material has been published in regard to epidemic encephalitis, in spite of the fact that the disease has not appeared in epidemic form during this period.

The third report covers the entire literature from 1930 to 1937. The work, moreover, done on the viruses that have been isolated in relation to epidemic encephalitis, on varied allied diseases and on vaccines is clearly outlined in preliminary chapters. The most important additions are those relating to human encephalitis caused by the viruses of Eastern and Western equine encephalitis, post-vaccinal encephalitis, postinfectious encephalitis, hemorrhagic encephalitis and various related diseases, such as lymphocytic choriomeningitis.

The book is adequately indexed and published in a convenient size and format. It is one that no worker in the field of virus diseases can possibly afford to be without.